



APOTHECARY OPTIONS

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More copies of this handout are available at
www.apothecaryoptions.com

HORMONE FACTS

Fundamentals of Bio-Identical Hormone Replacement Therapy (BHRT)

- Provide replacement with hormones that are identical to what the body produces. It's called Hormone Replacement Therapy --- Not Hormone Substitution Therapy. This is true in all areas of Endocrinology -- if the human hormone is available for replacement -- use it! Don't use synthetic hormones that **IMITATE** human hormones, use hormones that **MATCH** human hormones.
- Replace hormones via a drug delivery system that replicates natural secretion patterns. Topical administration mimics natural ovarian secretion better than any other method.
- **Replace with physiologic doses.** We know much how estrogen, progesterone, and testosterone are produced naturally. Physiologic doses cause the least interference with a woman's own production of hormones. Only replace hormones if there is a clear evidence of need as determined by a review of physical symptoms and baseline testing of hormone levels.
- Be Patient – Hormone imbalance does not occur overnight, and it will not resolve overnight. Correcting serious imbalances may take 3-6 months. Expect some adjustments and fine tuning of the replacement regimen.

How much total Estrogen, Progesterone, and Testosterone do most women produce in a day?

- Estradiol** - 0.07 - 0.5mg (70 – 500 mcg) per day depending on the day of the cycle. The highest estrogen release during the menstrual cycle occurs mid-cycle (typically increases starting on day 10 and peaks usually on day 12). Ovulation occurs around day 14. The next highest peak occurs on day 21. Many women report bloating when their estrogen is at the highest level. The lowest estrogen production occurs on days 1 & 28
- Progesterone**
 - 2-3mg per day in the follicular phase (days 1-14 of cycle)
 - 30 mg/day in the luteal phase (days 15-28 of cycle). Peak levels days 19-22
 - 300-400mg/day by the placenta during the last trimester of pregnancy
- Testosterone** - 0.25 - 2mg per day (average 0.5 - 1mg). Doses > 2mg have a tendency to cause increased body hair (in places you may not want it!)

How Much Testosterone do Men Produce?

- A normal male adult produces 4-7 mg of testosterone per day

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How Much Hormone Does the Body Produce Naturally?	Commercial Product	=	<u>Approximate Bioidentical Conversion</u>
<p style="text-align: center;"><u>Estradiol</u> Normal Body production =</p> <p>0.07 - 0.5mg per day depending on the day of the cycle</p> <p>Highest estrogen production comes mid-cycle (~days 12-14)</p> <p>Significant estrogen production in adipose tissue during menopause due to aromatization. Some heavy women produce more estrogen during menopause than thinner women do in pre-menopause.</p>	Premarin® 0.625mg oral (or Cenestin®)	=	Tri Est 5mg oral (Tri-Est recommended due to Premarin® containing 50% estrone)
	Premarin® 0.625mg oral (or Cenestin®)	=	Estrace® 1mg oral
	Estrace® 0.5mg oral	=	Bi-Est 2.5mg oral
	Estrace® 0.5mg oral	=	Bi-Est 0.315mg topical cream
	Estrace® 0.5mg oral	=	Vivelle® 0.05 mg topical patch
	Vivelle® 0.05 mg topical patch	=	Bi-Est 0.3125mg cream/day
	Estrasorb® (estradiol hemihydrate) 1.74gm packet One packet = 0.025mg estradiol	=	0.025 mg Vivelle® patch per packet or Bi-Est 0.1625 mg cream/day per packet
	EstroGel® 0.06% Each metered 1.25gm dose provides <u>0.75mg</u> of estradiol	=	This product is VERY strong. Monitor response. Each 1.25gm metered dose contains <u>0.75mg</u> of topical estradiol. Equivalent to 2-4 mg of oral estradiol per day.
	Estrace® 0.01% (estradiol) Vaginal Cream	=	Bi-Est 0.625 mg Vaginal Cream
	Vagifem® 0.025% (estradiol) Vaginal Cream	=	Bi-Est 1.25 mg Vaginal Cream
Estring® (estradiol 2 mg/90 days)	=	Bi-Est 0.125mg three times weekly - vaginally	
<p style="text-align: center;"><u>Progesterone</u> Normal Body Production =</p> <p>2-3mg per day in the follicular phase days 1-14 of cycle)</p> <p>30 mg/day in the luteal phase (days 15-28 of cycle)</p> <p>300-400mg/day by the placenta during the last trimester of pregnancy</p>	Provera® 2.5mg oral (medroxyprogesterone is a "progestin" Progestins should never be a substitute for natural progesterone)	=	Natural Progesterone 100mg oral (slow release)
	Prometrium® 100mg	=	Progesterone 10-15 mg cream/day
	Prometrium® 200mg	=	Progesterone 20-30 mg cream/day
<p style="text-align: center;"><u>Testosterone</u> Normal Body Production =</p> <p>0.25 - 2mg per day (average 0.5 - 1mg)</p>	Estratest® 1.25mg/2.5mg	=	Tri-Est 1.25mg + Testosterone 2mg cream
	Estratest® H.S	=	Tri-Est 0.625mg + Testosterone 1mg cream

- ➔ Topical creams & patches are significantly more potent than oral meds. Oral hormones are extensively metabolized by the liver. Topical hormones are not significantly metabolized. Topical doses are usually 1/5th – 1/10th of oral doses (assuming complete absorption) **Estradiol 0.5mg oral = Estradiol 0.05mg topical patch = Bi-Est 0.3125mg topical cream**
- ➔ Topical delivery mimics natural secretion patterns. Oral Progesterone is extensively metabolized and has a short half-life. Progesterone cream provides more sustained protection against unopposed estrogen than oral progesterone. Progestins are not the same as natural progesterone.
- ➔ Topical estradiol alone may not adequately relieve vaginal dryness. We recommend combining estriol with estradiol. Estriol (E3) is the estrogen reported to be most responsible for maintaining optimal bladder and vaginal health.
- ➔ Studies have shown that maximum osteoporosis protection occurs with 0.05 - 0.1mg/day of topical estradiol. Higher doses offer no increased bone benefits.

Relative Potency of the Three Primary Estrogens

- **Estradiol (E2)** is the predominant estrogen secreted by the ovaries and is the most potent.
- **Estrone (E1)** Estrone is produced by the oxidation of estradiol. After menopause, most estrogen production comes from the conversion of androstenedione (secreted by the adrenal cortex) to estrone (E1) in peripheral tissues by aromatization. Estrone is the most abundant circulating estrogen in postmenopausal women. Estrone is 12 times less potent than estradiol on endometrial tissue response. Estrone is more potent than Estriol. There are concerns that high levels of estrone may increase the risk of breast cancer. Premarin is composed of > 50% estrone.
- **Estriol (E3)** is a byproduct of estradiol and estrone and is 80 times less potent than estradiol on endometrial tissue response. Estradiol (E2) is estimated to be 1000 times more potent than estriol with respect to breast tissue proliferation. The highest concentration of estriol is found during pregnancy. Because estriol is the end-product of estradiol metabolism, it may accumulate with time. Of the three primary estrogens, estriol has the shortest binding time to estrogen receptors. Estriol is reported to be the most beneficial estrogen of all the estrogens for maintaining good bladder and vaginal health.

There are Significant Advantages of topical delivery

- The most significant reason to use topical delivery is that it **mimics natural secretion** patterns.
- All oral hormones are metabolized extensively through the liver (Note: there is some evidence that hormones prepared in oil capsules may be absorbed into the lymphatic system and therefore bypass a portion of the liver metabolism).
- Oral hormones stimulate the production of Sex Hormone Binding Globulin (SHBG) and thyroid hormone binding globulin (THBG). Stimulation of THBG results in decreased T4 → T3 conversion and development of subclinical hypothyroidism.
- Oral estradiol is extensively and rapidly metabolized to estrone. High levels of estrone appear following oral administration of estradiol.
- The skin metabolizes hormones only to a small extent. Topical delivery avoids the first-pass metabolism in the liver and allows for a more sustained delivery of hormones.
- Transdermal delivery produces therapeutic tissue concentrations of hormones at much lower doses. **Lower doses of hormones are used topically** (usually 1/5th – 1/10th of the oral dose is all that is needed to achieve the same results) – this is true for estrogen, progesterone, testosterone, and DHEA.
- Only minimal fluctuations in hormone levels occur because the skin acts as a drug reservoir. Systemic levels are maintained more consistently than with oral dosing.
- Topical creams can be dosed once or twice daily.
- Rotation of application sites is important to minimize the chance of antibody development to topical hormones.
- The best time to absorb the cream is after a warm shower or bath. Towel dry, and then apply the cream. Rub the cream in well for at least one minute – until area gets slightly warm due to rubbing.
- Be careful about skin-to-skin transfer with any topical hormones. Always wash hands thoroughly after application. Cover application site with clothing for 2-3 hours. Use particular care if touching babies and small children.
- The only way to achieve sustained progesterone levels in the body is with a topical cream formulation.
 - Oral progesterone, offers protection against unopposed estrogen but it does not provide the sustained levels that are achieved with a topical cream.
 - All oral progesterone products, including Prometrium[®], are significantly metabolized by the liver into various metabolites.
 - The half-life of oral progesterone in the bloodstream is very short (~ 60 minutes). Prometrium[®] peaks in approximately 3 hours and is almost entirely out of the system in 4-6 hours.
 - To provide more consistent blood levels, Prometrium[®] should be dosed every 12 hours, however this is not practical for most patients because the drug causes significant sedation.
 - The rapid metabolism of Prometrium[®] can occasionally result in spotting (especially in patients taking larger doses of estrogen) This is because the abrupt drop in progesterone levels (due to its rapid metabolism) tricks the body into thinking it's time for a menstrual cycle and some spotting may occur. Use of a physiologic dose of progesterone cream (which has more of a sustained effect in the body) tends to minimize the incidence of spotting.

Saliva Testing vs. Blood Testing

More than 95% of blood hormones in women and men are bound to specific proteins, which carry them throughout the bloodstream. The remaining amount (approximately 1 - 5%) represents your **free** (or *bioavailable*) hormones. As blood circulates around the salivary glands, your bioavailable hormones (those that are not bound by blood components) freely diffuse through the cells of the salivary gland and into the salivary ducts. Studies in the scientific literature have shown that there is a strong correlation between the levels of "free" hormones found in saliva and the bioavailable levels of hormones found in the bloodstream and tissues. The free portion of the hormone is what exerts an effect on the body. Free hormones can move throughout the body and into the cells of your organs and tissues to perform their designated functions. Protein-bound hormones are not fully biologically active. Some common blood tests only measure total hormone levels - which is the sum of the protein-bound portion *plus* the non-protein bound portion. These blood tests are unable to distinguish how much is free and available, versus how much is bound and unavailable. It is quite possible for a person to have a total hormone level in the "normal" range – yet still have a very low level of free hormone.

Saliva testing is becoming recognized as a non-invasive, reliable, and accurate way to measure free hormone levels and test for hormone deficiencies. Saliva testing only measures unbound (**free**) hormone levels. **Saliva testing is more accurate than blood testing for topically administered hormones** -- the preferred method for hormone replacement. For more information on saliva testing, visit www.salivatest.com

How often should levels be checked? The goal of saliva hormone monitoring is to assess your level of imbalance and help determine whether hormone replacement therapy or another form of intervention is appropriate. If you are already taking hormones, testing will allow you to adjust your individual dosage, thus optimizing benefits while at the same time helping to minimize risks. Hormone levels should always be assessed initially to establish baseline levels and determine a starting point. Once hormone balance is achieved, check levels yearly. Check more frequently if you are still experiencing symptoms of hormonal imbalance.

Women: Check your Estradiol, Progesterone, Testosterone, DHEA, and Cortisol levels

Men: Check your Testosterone, Estradiol, DHEA, and Cortisol levels

Hormones in saliva are very stable. Samples can be stored at room temperature for extended periods (a week or more) without any loss of activity. Samples are shipped to the testing facility by regular mail – there is no need for special refrigeration. Saliva testing is a covered benefit by some insurance companies – *check with the individual laboratory to find out specifics about insurance coverage*. Patients can avoid any insurance delays by paying the out-of-pocket cost of approximately \$30 per hormone level tested (this is about 70% less than the cost of blood testing). Fees are paid directly to the lab.

Apothecary Options receives no financial compensation or kickback for recommending Saliva Testing

Our bodies contain an estimated 60 trillion cells that all must communicate with each other. These cells respond to a special language that is orchestrated by our hormones. Hormones travel throughout the body and enter cells through receptor sites located on the cells. When a hormone attaches to a receptor it is similar to a key opening a locked door. Once inside the cell, the hormone gets to work, flipping switches and pulling levers that regulate mental and physical functions throughout the body. Hormones exist in harmony with each other. When our hormone levels are balanced in the right proportions, the body is happy and stable. When balance is lost, we become more susceptible to disorders and diseases (both physical and mental). Hormone imbalance is associated with every major disease that plagues Western society (cancer, heart disease, osteoporosis, and diabetes) and some medical experts think that hormone imbalance is a contributing factor in depression and certain types of mental illnesses.

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When Should Saliva Testing be Done?

- For menstruating females – Saliva testing should be done on day 19, 20, or 21 of cycle (where day 1 is always the first day of bleeding). Menopausal women and women who have had a hysterectomy (with or without ovary removal) – Saliva testing can be done any day. For Men – testing can be done on any day.
- Women that are currently on oral contraceptives should be off contraceptives for two full cycles before testing.
- For women with irregular periods: If you just had a period, count out 19 days from the first day of your period (day one is always the first day of bleeding) and collect saliva on that day. If you have not had a period for several months, collect your saliva on any day.
- If you are supplementing with hormones, make sure you have been taking them for a minimum of 2-3 weeks before testing your saliva.
- Avoid vigorous exercise the day before saliva collection if you are testing for cortisol. Gentle exercise (like the walking the dog) is okay, but strenuous aerobic workouts will alter your cortisol levels and make the test results less accurate.
- If you are using topical hormones, do not use them within 12-24 hours of collection if possible (see chart)
- Women who take cycled hormones (and who are not menstruating) should collect toward the end of the hormone treatment cycle. Example: If you take hormones 25 days out of the month, then collect saliva 3-4 days before the end of that treatment cycle.
- Women who take hormones every day, can test any day of the month
- Eating food or chewing gum will compromise your test results. Follow the collection instructions precisely.

Type of Hormone Dosage	Always collect samples in the morning . Within 1hr of waking, and before any food or drink	Optimal collection time
Oral Hormones (including oral progesterone)		8-24 hours AFTER last dose (optimal time is 8-12 hours after dose)
Topical Creams		12-24 hours AFTER last application (do not apply cream to face or neck)
Sublingual tablets / Troches		36 hours AFTER last dose
Transdermal Patches		For Bi-Weekly patch: 2-3 days AFTER applying patch
Vaginal Suppositories		12-24 hours AFTER last dose
Hormone Injections		Midpoint between injections

A Collection of Notes about Saliva Testing

- 0.5% of saliva volume is plasma.
- If a patient is on sublingual hormones, do not do saliva testing for 36 hours after the last dose, otherwise it will result in artificially elevated levels.
- When steroids are delivered through the skin, saliva hormone levels are more reflective of tissue levels than serum hormone levels. High saliva levels seen with creams are due to **HIGH** doses – not lab error
- Patients with periodontal disease can sometimes have false/misleading saliva results
- Salivary/Serum correlations are usually very good for hormones produced endogenously (by the body), however, salivary/serum correlation becomes a problem depending on the type of hormone administration:
 - Oral Delivery of Hormones → Serum overestimates hormone levels
 - Topical Delivery of Hormones → Serum underestimates hormone levels
- Saliva testing limitations – saliva testing can't be used to measure peptide hormones (FSH) or thyroid hormones
- When saliva test results come back, pay attention to the E2/Progesterone ratio. This ratio should be 50-200. When the ratio is less than 8, this is a good indicator of ESTROGEN DOMINANCE.
- Very difficult to achieve adequate progesterone levels with oral progesterone due to extensive metabolism and a very short half-life.

CPT CODES FOR SALIVA TESTING	
82670	Estradiol (E2)
82677	Estriol (E3)
82679	Estrone (E1)
84402	Testosterone (T)
82627	DHEA-S
82530	Cortisol

Many prescribers are now offering saliva testing in their medical offices. These are the billing codes that prescribers can use to receive reimbursement from insurance companies.

What about 24 hour Urine Collection to measure hormones?

- **Advantages:** Non-invasive. Ability to check a wide range of hormones. Provides a good estimation of total daily hormone production.
- **Disadvantages:** Inconvenient type of collection process. Urine collection is more reflective of metabolites (i.e. what is being thrown away) versus what is bioavailable and being utilized by tissues. Normal ranges are often too wide for accurate interpretation.

Female Hormone Patterns by Age

Teenagers – Anovulatory cycles are common. Low progesterone is very common. Estrogen dominance is common and is caused by too much estrogen in the luteal phase (2nd half) of the cycle. Teenagers can have high DHEA, which is locally converted in the skin to testosterone causing acne and oily skin. If you have adolescent daughters with mood and behavior changes → determine if it is menstrual cycle-related; do the changes occur in the two weeks before her period? If so, consider supplementing with progesterone cream 20-30mg twice daily from days 14-28 of cycle. The positive changes will be dramatic.

20-30 year olds – These women have the best hormone balance. They have mostly normal menstrual cycles and they are at their peak fertility period.

30-40 year olds – Begin to see subtle changes in cycles usually starting around mid-thirties. Early indications of estrogen dominance are starting to appear in many patients. These women are more at risk to the effects of estrogen dominance (uterine fibroids, endometriosis, and fertility problems). Decline in progesterone levels may put them at greater risk of breast cancer.

Peri-menopause (40-50) – Progesterone levels decline dramatically. Anovulatory cycles occur with irregular bleeding. Irregularity in periods starts to occur. Estradiol levels may actually increase in some women due to ovarian production combined with being overweight. Ovaries may secrete more testosterone. Functional hypothyroidism is common (normal TSH levels) but with weight gain, feeling cold, chronically tired, and diminished sex drive. These women need a complete hormone and thyroid work-up.

Menopausal (>50) – 40-50% drop in estradiol levels. Estrone (E1) levels rise due to the conversion of androstenedione to estrone in peripheral tissues. Progesterone and Testosterone production drop significantly. During menopause women start secreting higher amounts of adrenocortical androgens, which causes hirsutism (increased body hair - particularly noticeable on the face). Hormone balance can help correct hirsutism within a few months.

The Key is Balance!

Our bodies contain an estimated 60 trillion cells that all must communicate with each other. These cells respond to a special language that is orchestrated by our hormones. Hormones travel throughout the body and enter cells through receptor sites. When a hormone attaches to a receptor it is like a key opening a locked door. Once inside the cell, the hormone gets to work, flipping switches and pulling levers that regulate mental and physical functions throughout the body. Hormones exist in harmony with each other. When our hormones are balanced in the right proportions, the body is happy and stable. When balance is lost we become more susceptible to disorders and diseases. Hormone imbalance is associated with every major disease that plagues Western society (cancer, heart disease, osteoporosis, and diabetes) and may be linked to depression and mental illnesses.

Stress Effects on Hormone Balance

Stress leads to increased cortisol levels which causes

- ↑ estrogen dominance
- ↑ blood glucose and ↑ insulin resistance
- ↓ progesterone activity
- ↓ thyroid receptor activity (↓ conversion of T4 → T3)
- ↓ DHEA

Estrogen Dominance/Lack of Progesterone (Three key symptoms)

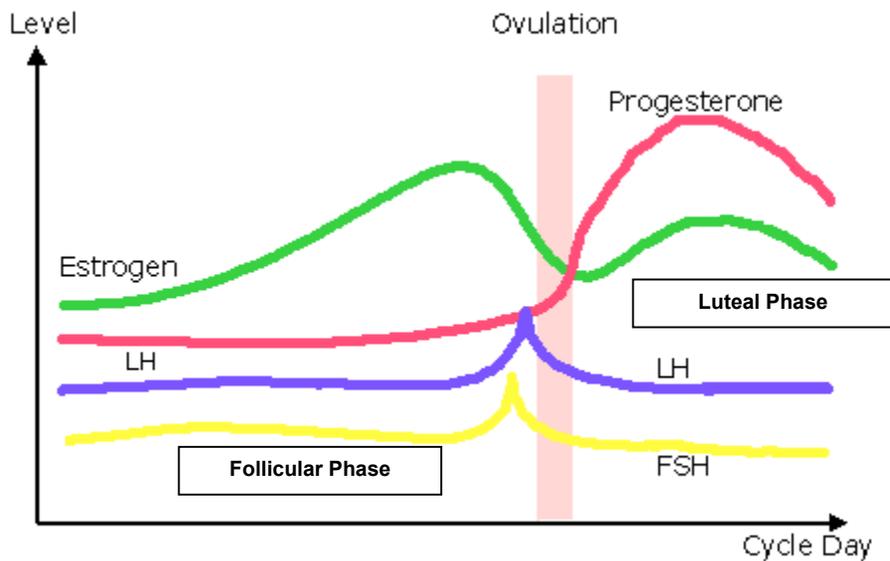
- Weight Gain
- Breast Tenderness
- Fatigue

Hormone	Deficiency Sign	Excess Signs
Estrogen	Vaginal Dryness, hot flashes, night sweats (vasomotor symptoms), vaginal atrophy, urethritis/urinary incontinence, pain during intercourse, dry skin, lack of mental sharpness, osteoporosis, interrupted sleep, less fullness of the breasts.	Rapid Weight gain (especially at the waist/hips), breast tenderness , migraines and headaches, water retention (puffiness), uterine fibroids, anxiety/panic attacks, heavy periods, nausea, fatigue, tingling of fingers (pins & needles). Excess estrogen can also suppress the activity of the thyroid gland.
Progesterone	PMS, depression, anxiety, bloating, and edema poor sleep; early AM waking, irregular periods	Dizziness, somnolence, acne. Adequate progesterone helps the thyroid gland.
Testosterone	Depression, fatigue, decreased libido, osteoporosis, decreased immunity, lack of muscle tone/strength, poor overall sense of wellbeing	Acne, oily skin, Rosacea, aggressiveness, increased sex drive, hair loss, anxious mood, rage, weight gain at the waist, high triglycerides, polycystic ovary syndrome
DHEA	Fatigue, depression, decreased immunity, autoimmune diseases, decreased sense of wellbeing	Acne, hair loss
Cortisol	Chronic fatigue, allergies, asthma, susceptibility to illness and infection, arthritis, fibromyalgia.	Sleep Disturbances , Muscle and bone loss, abdominal fat, elevated blood sugar, sugar craving, insulin resistance, high blood pressure, decreased libido, feeling of being “burned-out” impaired memory, irritability

Try to Avoid “SAMENESS”

Sameness occurs when a woman receives the exact same dose of HRT every day without any break or variance. Many experts believe that the human body does not like sameness. They believe that by varying the HRT dose, even slightly, it more mimics normal menstrual cycle variations that occur each month. Allowing periodic breaks is healthy for a woman. “Pulsed” delivery of estrogen and progesterone, the way that occurs naturally, enhances the functioning of the hormones in the body, and allows for smaller amounts of hormones to be used. Lower hormone doses translate to a decreased likelihood of unwanted side effects as well as a reduced impact on liver metabolism (caused by supplemented oral hormones). In theory, continuous application of hormones may serve to down-regulate receptors (makes receptors less sensitive), contributing to a general decrease in the activity of those particular hormones. By taking a break, or varying the dose, it allows hormone receptors in the body to be reset – mimicking what happens naturally in the body during a menstrual cycle. As long as the estrogen dose is not too high, there should not be any spotting or bleeding with this type of dosing.

4 Phases of a Normal Menstrual Cycle:



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The menses (bleeding or period): Commonly lasts from day 1 to day 5. (Day 1 is always considered the first day of bleeding) During this phase, if fertilization of the egg has not happened, the lining of the uterus, which is called the endometrium, comes away from the uterine wall. Blood and tissues pass out via the vagina. Most women bleed for between 3 and 5 days. The lining of the endometrium will end up about 1 mm thick at the end of the period. As well as the loss of the endometrial tissue, about 35 to 50 mL of blood is lost from the broken endometrial blood vessels in a typical period. This blood does not usually clot unless bleeding is very heavy.

The follicular phase: this phase is so-named because it is when the follicles in the ovary grow and form an egg. About 3 to 30 follicles grow between days 8 and 10. Each follicle contains an egg, but by days 10 to 14 one follicle has overtaken the rest and has reached the correct stage of maturity. During days 6 -14, the lining of the uterus is repaired and becomes thicker (refer to the diagram on the top of page 12). This phase is also known as the proliferative phase due to the build-up of the uterine lining. The build-up is stimulated by estrogen, which is secreted from the ovaries. By the time this process is complete the lining of the uterus will be approximately 3 mm thick.

Ovulation: A surge of luteinizing hormone (LH) occurs roughly just before day 14 in a 28-day cycle. This surge stimulates the mature follicle in one of the ovaries to release its egg (ovulation) 16 to 32 hours later. The other follicles over-ripen and break down. Estrogen also peaks during this surge. Some women can feel a pain on one side of the abdomen around the time the egg is released. This is known as 'mittelschmerz' – a German word translating as 'middle pain'. An egg is released from the right or left ovary at random and takes about 5 days to travel down the fallopian tube to the uterus.

The luteal phase: This phase follows ovulation and lasts from about day 15 to day 28. After the follicle ruptures and releases its egg, it closes and forms a *corpus luteum*. The corpus luteum secretes more and more progesterone, which acts on glands in the endometrium and causes them to make a secretion. The purpose of this secretion is to feed the embryo for a few days until a placenta has formed. Even if the egg is not fertilized and pregnancy has not happened, the secretion is still produced. The progesterone secreted by the corpus luteum causes the temperature of the body to rise slightly until the start of the next period (see diagram on bottom of page 12). This rise in temperature can be measured and plotted on a graph and gives a reliable indication of when ovulation has occurred. If the woman has not become pregnant the corpus luteum lasts about 14 days and then starts to break down. This is when progesterone production rapidly drops and the estrogen level decreases. This lack of hormones causes blood vessels in the endometrium to go into spasm and they cut off the blood supply to the top layers of the endometrium. Without oxygen and nutrients from the blood, the endometrial cells begin to die, tissue breaks down and there is bleeding from the damaged blood vessels and a new menstrual cycle begins on about day 28.

What Happens to the Cycle in Menopause? As the ovaries age, there is a gradual failure of the follicles to respond to FSH stimulation. The secretion of estrogen declines. The body's response to declining estrogen is to increase FSH production. Elevated FSH levels are one indicator that a woman is entering menopause. During this same time, the mid cycle LH peak is lost and anovulatory menstrual cycles (bleeding cycles but without ovulation) occur. As ovarian function further declines, ovulation ceases completely. The absence of a corpus luteum results in a reduction in progesterone secretion. Eventually estrogen levels become so low that menstrual bleeding becomes irregular and finally ceases. Declining estrogen and progesterone levels result in vasomotor instability (hot flashes, night sweats). During this time the body also starts secreting higher amounts of adrenocortical androgens, which causes hirsutism (increased hair - particularly noticeable on the face).

Ultimately, the decline in estrogen production affects the secondary sex organs. The breasts become smaller and lose their shape. The vulva and vaginal tissues become less vascular. Vaginal atrophy develops. A lack of natural lubrication causes painful intercourse and increased risk of infection. Eventually the ovary and uterus atrophy, and the endometrium basically disappears. Low estrogen levels after menopause are directly associated with osteoporosis with resulting weakness of the weight bearing bones and increased risk of fractures (especially hip and vertebrae).

The Five Most Common Ways to Prescribe BHRT

1. **Continuous-cyclic BHRT (also called sequential cyclic) – usually recommended for patients who are still menstruating and want to mimic a natural cycle.**

- Estrogen is given every day. Progesterone is added at the end of the cycle. Testosterone is given daily if needed.
- Progesterone (~15-40mg) is added to the regimen on days 12-26 or 16-26 (for a total of 10-14 days). Starting the Progesterone too early in the cycle may cause a woman not to ovulate. For ovulating women, use progesterone starting on day 15-16 of cycle and go until day 26. For non-ovulating women, begin on day 12 and go until day 26. Progesterone is typically given for 10-14 days. This therapy helps minimize the risk of endometrial hyperplasia that will occur in patients on estrogen-only therapies. The ratio of estrogen/progesterone should be approximately 1:20. In some patients with estrogen dominance you add a very low dose of progesterone (~ 5mg) to their estrogen cream and give it the first half of the cycle, then add a higher dose of progesterone at the end of the cycle.
- 80% of patients will have a "scheduled bleed" or menstrual cycle due to the drop in progesterone at the end of the cycle. This option is good for patients who are still having a period or those who want to continue with a period.
- Candidates = Peri-menopausal or pre-menopausal patients - these patients are still having a period and this therapy encourages a continued menstrual cycle and the regular shedding of the uterine lining as Mother Nature intended.
 - **Advantages** - mimics a normal cycle. Good choice for women who are still cycling
 - **Disadvantages** - Requires two different drug formulas/recipes due to the need for extra supplemental progesterone in the last part of the cycle. This increases the expense due to the use of two different products.

2. **Cyclic HRT**

- Estrogen +/- testosterone (no progesterone) is given on days 1-25 only. For peri-menopausal women, day 1 = first day of period. Progesterone added the last 10-14 days (days 11-25 or 15-25)
- With this type of delivery, there are 3-6 days at the end of the cycle where there is no therapy of any type.
 - 6 days = if a woman is using a calendar (30-31 day) month (i.e. menopausal women). Day 1 for menopausal women will be first day of calendar month.
 - 3 days = if a woman is still cycling and using a 28-day cycle (includes peri-menopausal women who are technically still cycling - although periods are becoming more irregular). Day 1 for these women will always be the first day of bleeding.
- Patient should have bleeding at the end of 28-31 days when progesterone is finished. In a non-ovulating woman (menopausal), this is called "scheduled withdrawal bleeding." While it resembles a period, it is not really a true menstrual cycle. Cyclic HRT causes most women to have predictable withdrawal bleeding, which can continue for years. Peri-menopausal women may tolerate cyclic HRT better than continuous HRT.
 - **Advantages:** May be acceptable in pre & peri menopausal patients. Cycled progesterone helps mimic a natural cycle. Helps minimize "sameness."
 - **Disadvantages:** Some patients complain of headache, hot flashes, and fatigue during the 3-6 days without any HRT. Requires the use of two different products.

3. **Continuous-combined HRT (No-Bleed Method):**

- Estrogen and Progesterone are given every day. However, the daily dose of progesterone is much lower than the daily dose in cyclic therapy.
- Irregular bleeding is more common with continuous HRT during the first year. With continuous HRT, one-third of women do not experience bleeding, many women stop monthly bleeding after 2 to 3 months, and most women stop monthly bleeding after 1 year of therapy.
- Continuous HRT causes fewer premenstrual-like symptoms as compared to cyclic HRT.
- Continuous HRT causes fewer side effects in women who are several years beyond menopause than in younger women.
- With continuous HRT, women who were treated with higher doses of progesterone had the fewest episodes of bleeding. Women with higher estrogen doses have a higher incidence of bleeding.
- Many HRT replacement specialists believe that menopausal women should be given continuous HRT in dosages that approximate the levels found in the follicular phase (1st half of the cycle) of women who are still cycling (refer to diagram on page 8).
 - **Advantages:** most women over 53, if given the choice, do not want to resume having periods. This regimen is a good choice for menopausal patients who are no longer cycling and who do not want to return to having periods
 - **Disadvantages:** Does not mimic a natural menstrual cycle. Important to maintain estrogen/progesterone balance – dosing adjustment not as easy when all ingredients are combined. Encourages “sameness”

4. **Continuous – Combined HRT with 3-4-day break at end of cycle – AVOIDS SAMENESS**

- Based on a calendar month (30-31 days). Starting on day one of calendar, Estrogen and Progesterone are given daily for 26-28 days, followed by a rest period of 3-4 days. Repeat the cycle the following month. This regimen is recommended for menopausal women. A variation of this is the “**Never on Sunday**” dosing schedule where HRT is given every day Mon-Sat and skipped on Sunday.
- There is a possibility of some breakthrough bleeding at the end of the cycle. If this occurs, lower the estrogen dose. Breakthrough bleeding usually stops after 3 cycles as the body adjusts to the regimen.
 - **Advantages:** The 3-4-day washout period, minimizes the problems that can occur with “sameness.” Sameness occurs when a woman receives the exact same dose of HRT every day without any break or variance. Many experts believe that the human body does not like sameness. They believe that by varying the HRT dose, even slightly, it more mimics normal menstrual cycle variations that occur each month. Allowing periodic breaks is healthy for a woman. “Pulsed” delivery of estrogen and progesterone, the way that occurs naturally, enhances the functioning of the hormones in the body, and allows for smaller amounts of hormones to be used. Lower hormone doses translate to a decreased likelihood of unwanted side effects as well as a reduced impact on liver metabolism (caused by supplemented oral hormones). In theory, continuous application of hormones may serve to down-regulate receptors, contributing to a general decrease in the activity of those particular hormones. By taking a break, or varying the dose, it allows hormone receptors in the body to be reset – mimicking what happens naturally in the body during a menstrual cycle. As long as the estrogen dose is not too high, there should not be any spotting or bleeding with this type of administration.
 - **Disadvantages:** Some women can experience headaches or a return of hot flashes if the rest period is greater than 4-5 days. A 3-day rest is sufficient and usually doesn’t cause any problems.
- **The significant advantage of this therapy is the reduced cost and ease of administration. All the HRT ingredients can be combined into one product and administered together.**

5. **Intermittent-combined HRT:**

- Give estrogen every day. Progesterone is added intermittently in cycles. 3 days on, 3 days off, throughout the month. The cumulative monthly dose of progesterone is about half of that on the continuous-combined pattern. This regimen seems beneficial to some women who cannot tolerate progesterone. Exposure to cycled progesterone throughout the month is enough to provide the protective benefits. Helps avoid issues of “sameness” by varying dosages every few days.
- **Disadvantages:** Requires a calendar to remember when to take progesterone. Requires two separate products, which increases the expense of the therapy. Possibility increases for breakthrough bleeding especially if the estrogen dose is high.

Estrogen Needs Based on Body Type

(Adapted from the book Natural Hormone Balance for Women by Uzzi Reiss)

Short, Voluptuous, Full-Breasted, (non-athletic) - These women produce more estrogen and function well at relatively higher doses. They are shorter because estrogen causes earlier bone closure when they are teenagers. They typically need a relatively higher level of estrogen replacement during menopause than other women do. These women also typically have low testosterone levels. These women tend to be happier due to the increased estrogen. This woman has 6 times as much estrogen as the tall, Twiggy, small breasted type women.

Tall, Thin, Small Breasted (Twiggy) - These women have grown taller because of less estrogen in their systems. They can operate on much less estrogen than some women can and replacement doses during menopause are usually lower. These women also typically have lower testosterone levels.

Athletic Woman: Tall, thinner, small-medium breasted. These women are physically stronger. They typically operate on more testosterone and not as much estrogen. They may not require as much estrogen replacement as the shorter, full-breasted woman.

Estrogen Checks (adapted from Natural Hormone Balance for Women by Uzzi Reiss):

Ring Check

- Adequate estrogen - rings on and off without much problem
- Lack of estrogen – rings slip off fingers too easily
- Excess estrogen – rings are difficult to remove

Breast Check

- Full, painful, or growing? - too much estrogen
- Lost some fullness, or seem to be droopy? - may need a little more estrogen

Mind and Mood Check - sometimes this can be a good indicator for a woman's estrogen levels.

- Irritable, uptight, but with a clear mind? - too much estrogen
- Foggy, confused, and a little depressed? - maybe need more estrogen

Sleep Check

- Night sweats – good indicator of lack of estrogen
- Hot flashes – good indicator of estrogen dominance

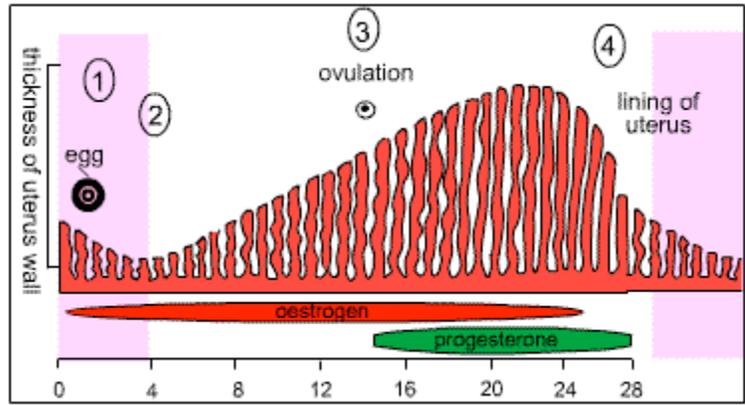
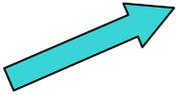
Too Much Estrogen?

- Breast tenderness
- Weight gain – especially around the middle and hips
- Craving for sweets
- Heavy periods (if still menstruating)

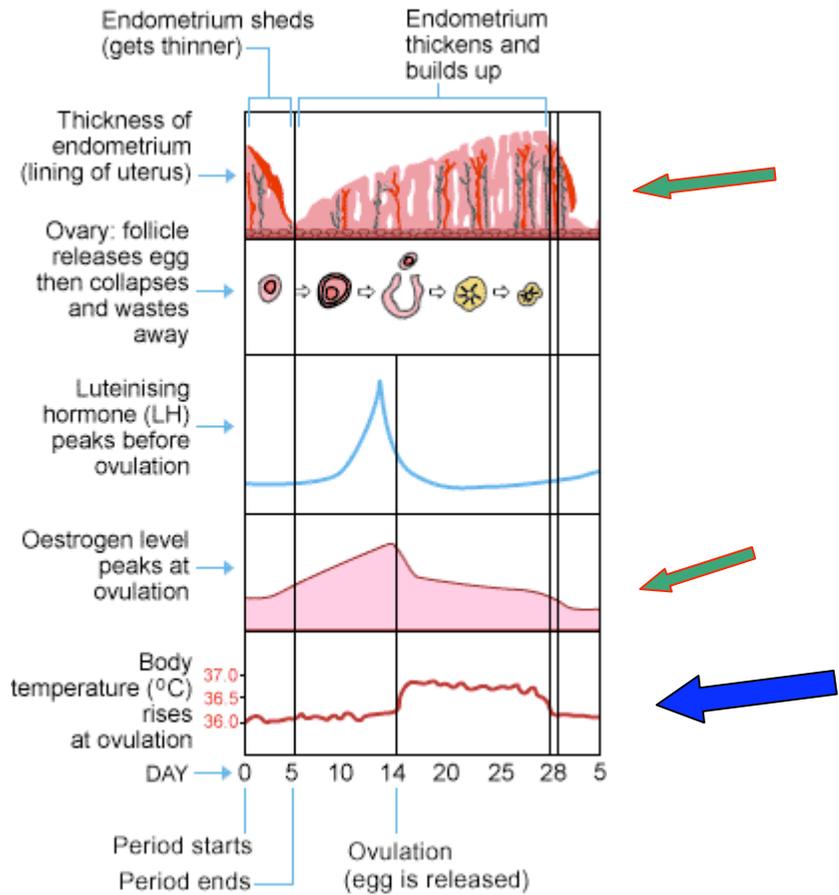
Not Enough Estrogen?

- Vaginal dryness and painful intercourse
- Less fullness in the breasts
- Frequent bladder or vaginal infections

More graphical representations of the menstrual cycle

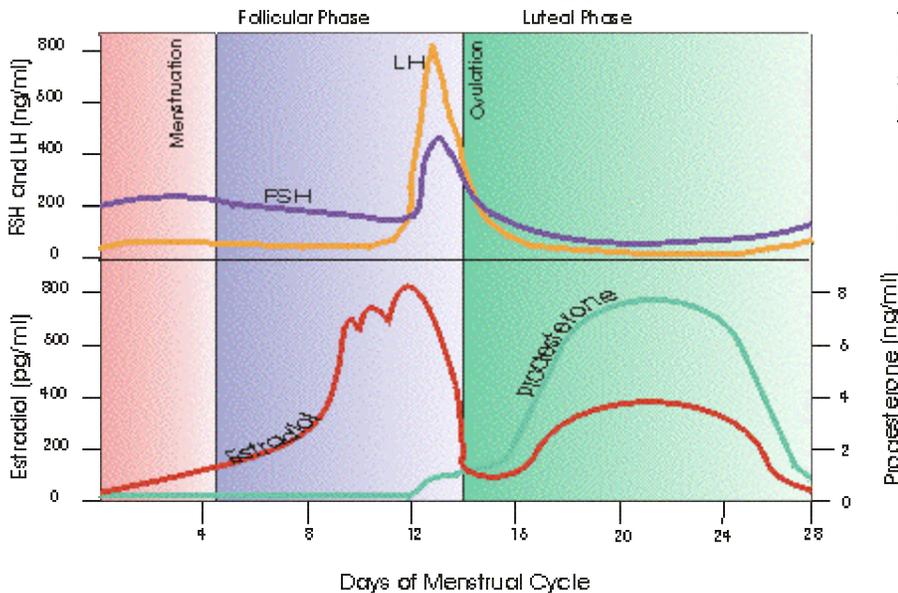


The diagram above shows the relationship between estrogen and the thickening of the uterine wall. The lining of the uterus sheds during the first few days of the menstrual cycle. Ovulation usually occurs around day 14. The first day of bleeding is always considered day 1 of the menstrual cycle.



This diagram shows the changes in body temperature that occur at ovulation (blue arrow). It also shows what happens to estrogen in the body and how the uterine lining thickens and then sheds during a normal cycle (green arrows).

Approximate Concentrations of Pituitary and Ovarian Hormones During Menstrual Cycle



This diagram shows the two phases of the menstrual cycle. The first half is referred to as the Follicular phase. The second half of your cycle is the Luteal phase.

Note how estrogen (red line) and progesterone (green line) have different peaks during a normal 28-day cycle.

How much total Estrogen, Progesterone, and Testosterone do most women produce in a day?

- Estradiol** - 0.07 - 0.5mg per day depending on the day of the cycle. The highest estrogen release during the menstrual cycle occurs on day 14 (ovulation), next highest peak occurs on day 21. Lowest estrogen production occurs on days 1 & 28
- Progesterone**
 - 2-3mg per day in the follicular phase (days 1-14 of cycle)
 - 30 mg/day in the luteal phase (days 15-28 of cycle)
 - 300-400mg/day by the placenta during the last trimester of pregnancy
- Testosterone** - 0.25 - 2mg per day (average 0.5 - 1mg). Doses > 2mg have a tendency to cause increased body hair (in places you don't want it!)

Suzanne Somers' Personal Bio-identical HRT Recipe

(From her book The Sexy Years)

- Estradiol (E2): twice daily every day of the month (oral) - no specific dosage given
- Natural Progesterone: Days 10-18 of the month (oral) - no specific dosage given
- Testosterone: In her book, she states that she uses 2.5mg drops twice daily. The upper limit on oral testosterone for women is usually around 4-6mg per day (testosterone dosages are much lower if she administers these drops sublingually). Doses in this range may cause skin changes such as acne or oily skin. Many women find that a topical dose of 0.5-2mg per day of natural testosterone can improve libido without side effects. Testosterone cream applied to the external vaginal mucosa works very well for improving libido.
- The Seven Dwarfs of Menopause (by Suzanne Somers) **Itchy, Bitchy, Sweaty, Sleepy, Bloated, Forgetful, and All-Dried-Up!**
- **Without knowing her specific HRT dosages, our professional guess is that Suzanne's personal recipe may be too high for most women. In her book, Suzanne states that she wants to continue having a menstrual cycle. The only way to achieve this in a woman of her age is to increase the estrogen dose substantially and then give progesterone on a cycle. Although it is not a true menstrual cycle (because there is no ovulation), women on this regimen will have a scheduled bleed. We do have had some women specifically request this type of regimen, however, for most women this is not our recommendation.**

A Collection of Notes about Estrogen

- **Normal Estradiol Production** - 0.07 - 0.5mg (70 - 500 micrograms) per day depending on the day of the cycle. The highest estrogen release during the menstrual cycle occurs around day 14 (ovulation), next highest peak occurs on day 21. Lowest estrogen production occurs on the days just before and after menstruation.
- One classic physical symptom of estrogen deficiency is **VAGINAL DRYNESS**
- **Low estrogen is usually the true culprit in patients with recurring urogenital problems such as vaginal dryness, increased UTIs, painful intercourse, and urinary incontinence.**
- Unopposed estrogen (without progesterone support) is a recipe for developing hypothyroidism
- Women with a low percentage of body fat may be at risk for low estrogen (higher incidence of osteoporosis). Menopausal women who are overweight can actually make more estrogen than thin premenopausal women.
- Estrogens exert a stimulating effect of the breasts, uterus, and brain. Estrogens prevent bone loss, dilate blood vessels, and maintain integrity of the urogenital tract (bladder and vagina). Too much estrogen promotes fat storage at the hips.
- Women that are stressed will burn up estrogen at a higher rate. When women are relaxed (i.e. on vacation), their estrogen needs go down. Women who are working out at the gym burn more estrogen.
- Many HRT replacement specialists believe that menopausal women should be given continuous HRT in physiological dosages that approximate the levels found in the follicular phase (1st half of cycle) of women who are still cycling.
- Smoking reduces estrogen levels. Cigarette smokers tend to reach menopause earlier than nonsmokers. Menopause is officially defined by the absence of menses for at least 12 months, in a woman more than 45 years of age.
- Studies have shown that the benefits on bone health disappear after short-term hormone use is discontinued. Use of estrogen for 3 to 5 years to relieve symptoms of menopause, followed by a discontinuation of therapy, did very little to prevent fractures from osteoporosis in women when they reached ages 75 to 80. These studies suggested that women, who take estrogen to maintain bone density, must continue taking estrogen to preserve the positive effects on bone health.
- When taking estrogen, if the initial good results fade and symptoms worsen, the starting dose was likely too high! Take a break from it, get some saliva testing done, and consider adjusting the dose downward.
- If patients are getting into an upward spiral of dosing (the need for higher and higher doses) the following factors should be looked at: absorption (rotate application sites), current dose is already too high, other hormone balances exist (low thyroid, high cortisol), stress, or nutritional issues.
- When applying an estrogen vaginal cream to a patient with an intact uterus, it is always recommended that a low dose (5-10mg/day) of progesterone be included to protect against uterine cancer.
- Women using vaginal estrogen need to use it during times of the day when they will not expose their partners to estrogen. There are numerous case reports of women using estrogen cream as a vaginal lubricant immediately before intercourse. Their partners end up getting high-level exposure to estrogen. We recommend apply vaginal estrogen in the morning or waiting 4 hours before any sexual activity.
- It has been established that estrogen decreases the risk of Type-2 diabetes (estradiol helps improve the body's responsiveness to insulin). Estrogen also decreases the risk of colorectal cancer, delays the worsening of symptoms of Parkinson's disease, improves sleep in women with insomnia, and improves balance and decreases the risk of falls in older postmenopausal women (source: HRT The Answers – by Pamela Wartian Smith, MD).
- Alcohol markedly increases estrogen levels in women. The effects can occur within 10 minutes. A half glass of wine can increase estradiol levels by 100% (source "Natural Progesterone Cream" by Norman Shealy, MD)
- Consider estrogen the "gas pedal" and natural progesterone as the "brake pedal" for hormone balance.
- **50% of women taking synthetic estrogen replacement quit after one year** because of undesirable side effects – primarily weight gain, irregular bleeding, breast tenderness, or bloating. These side effects are caused by **ESTROGEN EXCESS**. Women whose hormones are in balance (with physiologic doses) do not put on weight. (source "HRT: The Answers" by Pamela Wartian Smith, MD)
- Even low-dose birth control pills contain more estrogen and progestin than is typically required for treatment of perimenopause or menopause.
- There is considerable evidence that estriol (E3) may protect a woman against breast cancer because it blocks Estrone (E1) by occupying estrogen receptor sites on the breast. High levels of Estrone have been linked to breast cancer. Estriol has the shortest binding time to estrogen receptors and is reported to benefit the vagina and bladder more than estradiol (E2).
- Don't rely on FSH levels to indicate need for estrogen. FSH is an indicator of ovarian estrogen signaling and is a predictor of menopause. FSH does not accurately determine estrogen levels and does not account for non-ovarian sources of estrogen (such as adipose tissue). Follow-up a FSH level with saliva testing.

- Estrogen dominance has worsened in the last 40 years due to pesticides (many pesticides have estrogenic-like effects), microwaving of plastic containers, hormone-fed beef and poultry, contaminated water supplies, and high carbohydrate diets (leads to ↑ insulin)
- Women ages 20-30 have the best hormone balance. This is because estrogen production is not as high as it was in their teenage years and progesterone production has not started to drop off. Peak fertility occurs in women age 20-30.
- Obesity leads to higher levels of estrone (E1), the estrogen most associated with breast cancer.
- By age 60, nearly 1 in 3 women in the US have had a hysterectomy. The average age at the time of the operation is 42. More than three-fourths of all women who have a hysterectomy are between 20 and 49 years of age. **Source: American College of Obstetricians and Gynecologists (ACOG).** The percentage of American women who have a hysterectomy is much higher than the percentage of European women having a hysterectomy. For example, American women are twice as likely to have a hysterectomy as women in England and four times as likely as Swedish women.
- A recent study shows that the common practice of prophylactic removal of ovaries (oophorectomy) during hysterectomy for benign disease increases the overall mortality risk for women, especially those 65 years and younger. **(Parker WH et al. Ovarian conservation at the time of hysterectomy for benign disease. Obstetrics & Gynecology. 2005; 106(2): 219-226).**
 - Compared with women ages 50 to 54 who retained their ovaries, those undergoing oophorectomy without estrogen therapy were more than twice as likely to die from coronary heart disease, the leading cause of death among women. Overall, women undergoing oophorectomy before age 55 had about 8.5% increase in mortality compared with ovarian conservation. Women with oophorectomy before age 59 had nearly 4% increase in mortality
 - In the same comparison, women undergoing oophorectomy without estrogen therapy were 50% more likely to die from hip fracture – highlighting the positive effects that estrogen has on the prevention of osteoporosis.
 - The researchers suggested that the residual hormones produced by the ovaries after menopause may be important in protecting against heart disease and osteoporosis, especially for women who choose not to take hormone therapy.
 - The researchers conclusion – leave the ovaries in whenever possible.
- Here is an interesting fact about breast cancer: “90% of postmenopausal women who develop breast cancer, have never taken any kind of hormone replacement therapy” **(source “HRT: The Answers” by Pamela Wartian Smith, MD)**
- Another important fact is that breast cancer can grow for many years before it is detected by mammography – some experts suggest it takes 10 years of growth before breast cancer is finally detected. Women who have had children are usually at a lower risk for breast cancer than women who have never been pregnant – this may be due to a protective effect resulting from high levels of progesterone that are experienced during pregnancy.
- Premarin® (horse estrogen) has many negative effects on a woman’s body including: affects liver synthesis of proteins; leads to unnaturally high levels of estrogen metabolites; increases production of SHBG (sex hormone binding globulin) and thyroid hormone binding globulin, and increases production of C-reactive protein (a cardiac risk factor). Premarin® is composed of ~ 50% Estrone – an estrogen linked to breast cancer.
- Women taking Premarin® have the most difficult converting to BHRT. Premarin® has metabolites with very long half-lives. It can take several months for hot flashes to subside. Need to use Tri-Est (because it has a higher Estrone content which is found in Premarin®) These patients are advised to reduce caffeine intake, quit smoking, reduce stress through exercise, increase intake of Omega 3 fatty acids (fish oil capsules work well) and use Milk Thistle (300mg orally twice daily) to help detoxify their liver of the Premarin® metabolites. They should also increase fiber intake, and eat more cruciferous vegetables (high in I3C) which helps eliminate estrone metabolites. MSM (methylsulfonylmethane) is another ingredient found in many fresh foods. MSM also helps encourage the clearance of estrogen.
- Fibromyalgia may be due to estrogen dominance and progesterone deficiency. Often fibromyalgia develops when women are in their 30s-40s. These women often have fertility problems which may be caused by hormone imbalance – specifically progesterone deficiency. Saliva testing will help determine hormone balance.
- Oral estradiol is extensively metabolized, primarily to estrone. Hormone replacement with oral estradiol doses greater than 0.5mg (even though estradiol it is a natural hormone) results in excessive exposure to Estrone which is thought to be linked to breast cancer.
- Results of a 2-year controlled study show that maximal osteoporosis prevention occurs with topical estradiol doses of 0.05 mg (50mcg) per day. Higher doses of estrogen do not offer more osteoporosis protection.
- During menopause, women who still have their ovaries experience an overall drop in estrogen by 40-50%. Several studies are showing that even with this drop, a majority of women still have normal amounts of estrogen. What they are really lacking is progesterone support.

- Estriol (E3) is very effective when vaginal dryness is present. Use the lowest effective dose. Sometimes estradiol alone is not enough to correct vaginal dryness. We have plenty of experience with patients on therapeutic amounts of estradiol (patch or pill) that still have some vaginal dryness issues. Starting these patients on a low dose of Estriol usually corrects the problem.
- Some women crave chocolate to help with PMS. Chocolate craving is often due to a magnesium deficiency.
- When women first start on estrogen, “priming” is often necessary. Use higher doses for the first two weeks and decrease the dosage.
- All HRT requires a gradual tapering period (over at least one month) when a woman decides to discontinue treatment.
- After menopause, most estrogen production comes from the conversion of androstenedione (secreted by the adrenal cortex) to estrone (E1) in peripheral tissues by aromatization. Estrone is the most abundant circulating estrogen in postmenopausal women. Estrone is less potent than estradiol but high levels are linked to breast cancer.
- Estrogen – promotes endothelial repair, lowers fibrinogen, inhibits vasoconstrictors, has antioxidant effects and improves lipid profiles in patients (↑ HDL - good cholesterol and ↓ LDL – bad cholesterol)
- Do not be misled by people who would have you believe that estradiol cream cannot be absorbed through the skin because estradiol is “too big of a molecule.” Sex hormones are low molecular weight, highly lipophilic molecules that readily penetrate through the skin. In fact, estradiol is the one of the smallest of the sex hormones. Refer to the chart below for the molecular weights (relative size) of the various sex hormones. **All** of these are readily absorbed through the skin in gel, cream, or lotion formulations. Note: we include the molecular weight of estradiol hemihydrate (Estrasorb®). This is a commercially available topical, non-alcoholic emulsion product. Its molecular weight is greater than plain estradiol. Do you think the FDA would approve it if it was not able to be absorbed through the skin? Progesterone cream has been available for the more than 10 years – progesterone is a bigger molecule than estradiol and is readily absorbed and there is scientific data to prove it.

Molecular Weights of the Various Hormones	
Hormone	Molecular Weight (g/mol)
Estradiol (E2)	272.39
Progesterone	314.47
Testosterone	288.39
DHEA	288.43
Estrone (E1)	270.37
Estriol (E3)	288.39
Estradiol hemihydrate (Estrasorb®)	281.4
Fentanyl patch	336.5

Dr. David Zava – founder of ZRT labs in Oregon, has done some outstanding work looking at hormone profiles of women and men and how they correlate with specific cancer risks. The following table is a summary of his findings

Analysis of Hormone Profiles and Risk of Cancer	
Increased Risk of Breast Cancer in Women	Increased Risk of Prostate Cancer in Males
High Estradiol (E2)	High Estradiol (E2)
Low Progesterone	Low Progesterone
High Testosterone	Low Testosterone
Low DHEAS	Low DHEAS
High Night Cortisol	High Night Cortisol

From the book What Your Doctor May Not Tell you about Breast Cancer by John Lee and David Zava (founder of ZRT labs)

Why do Women Experience Hot Flashes?

Most women will agree that the most common and irritable symptom of menopause are hot flashes. Hot flashes and night sweats are reported to occur in 75% of menopausal women. Hot flashes usually begin during the two years preceding menopause. 20% of women find them completely intolerable. Hot flashes appear to be more common in African American women than in white, Hispanic, Japanese, or Chinese women.

Hot flashes usually wane over time, but in some individuals they may continue indefinitely. Women who suffer hot flashes may also complain of symptoms such as depression, anxiety, and difficulties with sleep and sexual function. Hot flashes are most disruptive at night. A change in body temperature is often associated with frequent awakening which can lead to chronic fatigue, irritability, mild depression, and changes in memory and attention span. For many women, hot flashes and associated insomnia are disabling.

The physical manifestation of a hot flash starts with a sensation of pressure in the head, progressing in intensity until the actual flush occurs. Hot flashes are frequently accompanied with heart palpitations. The flush itself begins in the head and neck area, then passes, often in waves, over the entire body, as a feeling of warmth or burning. Next, an immediate outbreak of sweating occurs involving the entire body, especially the head, neck, upper chest, and back. An episode may last a few seconds or several minutes (the average hot flash lasts approximately 4 minutes). A cold, clammy sensation concludes the hot flash. Hot flashes tend to come in bursts and may be brought on by stimuli such as eating, exercise, alcohol or caffeine consumption, or simply lying under a blanket. Both stressful and non-stressful events can trigger hot flashes. In many women, there is a "premonition" or "forewarning" that precedes the hot flash by several seconds.

Although hot flashes are common, their exact cause is not entirely understood. We know that estrogen is highly effective for the treatment of hot flashes. **However, hot flashes are not caused by a lack of estrogen.** If this were true, a 70 year old woman would experience more hot flashes than a woman in her 50's – and we know this is not the case. Hot flashes are more closely related to declining and fluctuating estrogen levels than with absolute levels. An older woman clearly operates on much less estrogen than a younger woman, however her body has adapted to the lower levels and she doesn't experience as many hot flashes. Interestingly, women born without ovaries and girls who lose their ovaries before puberty never get hot flashes...but if these women are given estrogen supplementation for over 1 year, and the estrogen is quickly stopped, they will experience hot flashes.

Estrogen influences the *hypothalamus*; the area in the brain that regulates body temperature. During perimenopause, ovarian function is intermittent, with periods of diminished estrogen production followed by sudden spikes. On days when a woman is producing enough estrogen she feels just fine. However, on other days, when her estrogen levels swing lower, she is more susceptible to having a hot flash. When estrogen levels fluctuate and decline, the hypothalamus, releases a trigger substance (the exact substance(s) has yet to be identified) that results in *thermoregulatory instability*. Thermoregulatory instability means the body's internal thermostat gets mixed up -- triggering a warming and sweating sequence -- an effort by the body to stabilize what it perceives as a change in internal temperature.

After the trigger substance is released, there are immediate changes in brain chemicals and hormones. Hot flashes are accompanied by abrupt increases in plasma epinephrine (150% increase) and decreases in norepinephrine (40% decrease). Epinephrine and norepinephrine are catecholamines (stress chemicals). An increase in luteinizing hormone (LH) is associated with most hot flashes. A woman's heart rate can increase by 10-20 beats/min just before the onset of the flash. Vasodilation occurs in the blood vessels, and skin temperature increases by a few degrees.

Lifestyle and psychological factors can increase the number and severity of hot flashes that a woman experiences. In fact, women with a high level of anxiety had nearly five times the number of hot flashes as those who tested lower on the anxiety scale. Women who smoked experienced twice the amount of hot flashes as non-smokers (smokers have increased estrogen in their stool – lower overall estrogen) and being overweight increases a woman's chances of having hot flashes.

One more important point – If a woman starts taking estrogen and experiences initial relief, and then her hot flashes gradually return → the chances are her starting dose was too high!

Here are some tips to cope with hot flashes naturally.

- Dress in layered clothing, preferably cotton, since natural fibers allow your skin to breathe. When you feel a flash coming on, you can simply shed layers to cool off. Since some flashes are followed by chills, it can be helpful to have a sweater to put back on.
- Limit substances that may act as triggers: caffeine, alcohol, spicy foods, diet pills, hot tubs, stress.
- Limit your intake of red wine, chocolate, and aged cheeses, which contain a chemical that can affect your body's thermostat and can trigger a hot flash.
- Drink plenty of water. Keeping well hydrated can help modulate your body temperature. Keep a supply of cool water nearby, even at night beside your bed. Adequate fluid intake can also help improve symptoms of vaginal dryness.
- Use lighter blankets or a fan near your bed to deal with hot flashes at night.
- Other self-help behavioral methods include practicing self-acceptance (remind yourself — out loud, if necessary — that this is a temporary symptom of menopause and perfectly normal), tracking the emotions and situations that precede a flash (thus putting some degree of self-control back into the equation) and trying to keep a sense of humor (share funny moments with friends who are also going through the transition).

Rebalancing a woman's hormones is the most effective way to control night sweats and hot flashes

Risk Factors for Osteoporosis

Fact: Estrogen provides protection against osteoporosis

- Gender – women are more at risk than men
- Age >65
- Ethnicity – Caucasian and Asian women are at higher risk
- Body Size – small frame, low body weight (< 125 pounds) are at greater risk
- Family history – If your mother has osteoporosis you are at a higher risk
- Low calcium, low phosphorus, low vitamin D diet/intake
- Smoking, excessive alcohol consumption, high caffeine consumption
- Sedentary lifestyle and/or prolonged immobilization
- Medications such as corticosteroids, heparin, gonadotropin releasing hormone (GnRH) analogs
- Falls, prior hip fractures or any type of fracture after age 50
- Predisposing medical conditions such as renal failure, hyperparathyroidism, or malabsorption
- Early onset of menopause or hysterectomy (with removal of ovaries)
- Results of a 2-year controlled study show that maximal osteoporosis prevention occurs with topical estradiol doses of 0.05 mg (50mcg) per day. Higher doses of estrogen do not offer more osteoporosis protection.
- Osteoporosis prevention effects stop when estrogen therapy stops.

A Collection of Notes about Natural Progesterone

- **Progesterone Production in Women**

- 2-3mg per day in the follicular phase (days 1-14 of cycle)
- 30 mg/day in the luteal phase (days 15-28 of cycle)
- 300-400mg/day by the placenta during the last trimester (last 3 months) of pregnancy
- Post-menopausal women typically need only about 10-20mg of natural progesterone per day
- The main hormonal change that occurs after menopause is not estrogen decline, it is loss of progesterone. While estrogen levels drop 40-50% at menopause, progesterone levels decline by almost 100%.
- Progestins are not the same as natural Progesterone. Progestins are patent-protected chemicals produced by drug companies that attempt to mimic some of the effects of natural progesterone. Unfortunately, these chemicals do not possess the same molecular structure as natural progesterone and the body is smart enough to know the difference.
- Progestins decrease the protective effects of estrogen on the heart. Natural progesterone is a coronary vasodilator (heart healthy hormone). Medroxyprogesterone (Provera®) is a coronary vasoconstrictor (unhealthy for the heart). Why use synthetic molecules that mimic progesterone when you can just use progesterone?
- Younger women with lots of unopposed estrogen do very well when given progesterone in the last 10-14 days of their cycle. In these women, it has a relaxing and calming effect. The younger the patient, the higher the dosage of progesterone that can be prescribed.
- According to Uzzi Reiss (Natural Hormone Balance for Women), 50% of older women, who have not been exposed to estrogen in the past few years, react to progesterone as if it was a toxic drug, because it causes a down regulation of estrogen receptors. Down regulation means that the receptors are less responsive to estrogen. These women develop panic attacks and can feel depressed. The administration of progesterone is causing their estrogen levels to drop further. These women need estrogen alone for 30-60 days, and then slowly add a **low** dose of progesterone (not high doses).
- Women who have had hysterectomies can still benefit from progesterone. There are still many prescribers who believe that hysterectomized women do not require progesterone supplementation because they no longer have a risk of endometrial hyperplasia or endometrial cancer. Progesterone receptors are located throughout the body, not just in the uterus. Progesterone is especially beneficial in reducing the risk of breast cancer.
- Generally accepted that the ratio of Bi/Tri-estrogen to natural progesterone to minimize risk of endometrial cancer should be approximately 1:20
- High dose progesterone cream (>100 mg/day) may accumulate. Symptoms of progesterone excess may go unrecognized for months. When the cream is stopped it may take 3-6 months for progesterone levels return to baseline. Overdosing of progesterone can cause down-regulation of receptors and loss of effectiveness. High doses of progesterone can cause bloating. Don't think of progesterone as being without side effects. Large topical doses of progesterone can cause headache, weight gain, fatigue, water retention, and depression. Excessive dosing can result in abnormally high levels after only 15 days of application.
- Stay away for OTC progesterone creams unless you have no other options (i.e. your doctor will not give you a prescription). Some work well, but many are manufactured by questionable companies with poor quality standards. Some of these creams have been found to be contaminated with estrogenic substances and some do not even contain real progesterone. Compounding pharmacies prepare the best creams from pure, pharmaceutical-grade ingredients. Not only that, our progesterone cream is less expensive than any progesterone you can buy in the store.
- **Progesterone causes more drowsiness when taken orally than when applied topically**. Women that are having a difficult time sleeping can benefit from taking oral progesterone at bedtime. Oral progesterone is converted into several metabolites that work on the GABA receptors in the brain, causing relaxation and sedation. Women whose sleeplessness is worsened by elevated PM cortisol levels can especially benefit from the balancing effects of natural progesterone.
- Menstruating women with symptomatic **PMS** (cramps, crying, and bitchiness) typically have estrogen dominance caused by a decreased amount of progesterone relative to estrogen. Supplementation with natural progesterone during the last 10-12 days of their menstrual cycle can improve PMS symptoms dramatically. Some of these women can also benefit by using a low dose (5-10 mg) of progesterone in the first half of the cycle, followed by a higher dose (20-40mg) during the last half of the cycle.

- According to new research by Dr. Kenna Stephenson (her book is called *Awakening Athena*); progesterone supplementation helps to normalize C-reactive protein (a cardiac risk indicator) over a period of several months.
- One of the reasons progesterone is able to control hot flashes is because it helps suppress the production of catecholamines in the adrenal medulla. Many physicians believe that catecholamine release is partially responsible for hot flashes. Exercise stimulates catecholamines and can trigger hot flashes.
- What are we aiming for when using progesterone for endometrial protection? We want the endometrial tissue to be non-atrophic, non-proliferative, and non-secretory. Low dose topical Progesterone (20mg/day) provides this. Interestingly Provera® (medroxyprogesterone) causes endometrial atrophy -- natural progesterone does not.
- Before you consider surgery for uterine fibroids – discuss with us about using natural progesterone. Try using progesterone cream (30mg twice daily, 21 days of the month). Eliminate all estrogen sources in diet. Do this for 6 months and see where you are. Progesterone will help shrink small fibroids.
- In a study by French scientists showed that topical progesterone applied to 1150 women with fibrocystic breasts decreased their risk of breast cancer (Plu-Bureau G, et al. *Cancer Detect Prev* 1999)
- Women who have had children are usually at a lower risk for breast cancer than women who have never been pregnant – this may be due to a protective effect resulting from high levels of progesterone that are experienced during pregnancy. However, women who have children after age 30 are at a higher risk than women who had children earlier. Earlier progesterone support may be a key since the incubation period for breast cancer is at least 10 years.
- Many women notice that during pregnancy they have fewer allergies and see remission of autoimmune diseases such as rheumatoid arthritis and lupus. This is possibly due to progesterone's natural anti-inflammatory and immune supporting properties.
- Fibromyalgia has an autoimmune component and may be due to estrogen dominance. Check hormone balance with a saliva test. If progesterone deficiency is present, try treating with Progesterone.
- Dr. Kenna Stephenson (*Awakening Athena*) says that pre-adolescent women and women in their 30-40's who develop new onset seizures should have progesterone levels checked. Progesterone has neuron-inhibitory effects – meaning that it lowers the stimulus for seizures. In Dr. Stephenson's experience, she found that many of these women had a progesterone deficiency. When she supplemented these patients with natural progesterone, their seizures were eliminated!
- Low progesterone is common in teenage females. Estrogen dominance is also common.
- Giving progesterone too early in the cycle will suppress ovulation (birth control effect)
- There are many instances of teenage girls being prescribed anti-depressants when in fact they might just need progesterone supplementation during the last half of their cycle. Saliva testing will show this.
- Progesterone enhances thyroid function activity. Progesterone supplementation will improve thyroid balance. The ovaries need T3 to be able to produce progesterone. Stress can decrease T3 levels, which in turn will decrease progesterone production.
- Progesterone is antagonistic to hypercortisol (too much cortisol) states. In other words, if you have elevated cortisol levels, you can benefit from the balance provided by using natural progesterone.
- For menstruating women, use a lower dosage of progesterone the first half of the cycle (5-10 mg). Double or quadruple that during the second half of the cycle. Younger women can tolerate much more progesterone than older women. Use physiologic doses.
- In men with gynecomastia, 2.5 – 5 mg of progesterone per day can help. A low dose of progesterone is also being studied in men with prostate cancer and in men with hair loss because of its ability to block the conversion of testosterone to DHT (the testosterone metabolite that is reported to worsen both conditions)
- Hormone Replacement Therapy (HRT) is replacing what is missing with the authentic human molecules. Using synthetic hormones (progestins) or estrogen should be called Hormone Substitution Therapy. Your body knows the difference. The failed WHI trial was a study of Hormone Substitution Therapy. Bio-Identical human hormones are available – there should be no excuses for not using them for replacement therapy.
- There is a gene in the body known as the p53 gene. The p53 gene is a type of cancer fighting gene that promotes **apoptosis**. Apoptosis is the body's natural process of getting rid of unwanted cells. P53 promotes "suicide" or apoptosis of cells with defective or abnormal DNA. There is a lot of current

research on apoptosis. Too much apoptosis causes cell-loss disorders (possibly linked to diseases such as Alzheimer's and Parkinson's) whereas too little apoptosis results in uncontrolled cell proliferation (namely **cancer**). Natural progesterone upregulates the p53 gene which promotes orderly apoptosis. This is one of the reasons why natural progesterone is thought to protect women against both breast and endometrial cancers.

- Women who underwent breast cancer surgery during the luteal phase of their cycle (when progesterone levels are naturally the highest) had a **2X** greater long-term survival rate than women who had surgery during the follicular phase (1st half of the cycle). Progesterone helps reduce estrogen's influence on breast tissue. Reference: PE Mohr et al, Brit J. Cancer 73: 1552-1555 1996 *Serum Progesterone Levels at Time of Breast Surgery and Long-Term Survival in Node Positive Patients*
- Researchers looked at estrogen levels in breast tissue before and after progesterone topical administration. They found that the application of progesterone had the ability to displace estrogen out of the breast tissue, thus resulting in lower estrogen levels. This is a protective effect by progesterone on breast tissue, and can reduce the potential for developing breast cancer. (reference Chang, K.J. de Lignieres B. Fertile Sterility 63:785-791 1995 "Influences of Percutaneous Administration of Estradiol and Progesterone on Human Breast Epithelial Cell Cycle")
- Many researchers believe that the reason why some women develop breast cancer is due to the presence of estrogen without the balancing effects of progesterone. Remember, progesterone levels drop significantly starting around age 35, while estrogen levels may remain normal until women are in their mid-late 40's. During this 10-15 year period women are at a greater risk of developing breast or endometrial cancers. Another important fact is that breast cancer can grow for many years before it is detected by mammography – experts suggest it takes 10 years of growth before a cancerous breast lump is large enough to be detected.
- **The only way to truly achieve sustained progesterone levels in the body and mimic ovarian secretion patterns is by using a topical formulation.**
 - **There is no commercially available natural progesterone patch.** There are some patches that contain a progestin (Climara Pro[®] - for instance, contains estradiol plus levonorgestrol (a synthetic progestin)). **Remember – synthetic progestins behave much differently in the body than natural progesterone. Stay away from them!**
 - Oral progesterone products (including Prometrium[®]) are significantly metabolized (~ 90%) by the liver into various metabolites. The half-life of oral progesterone is very short (<1 hour in the blood).
 - The peak effects of Prometrium[®] occur in 2-3 hours, followed by a rapid decline in serum levels. Most of the drug is completely out of the bloodstream within a few hours.
 - Some women report breakthrough bleeding when using Prometrium[®]. The reason for this is that the rapid drop-off in progesterone levels (due to the rapid metabolism) causes the body to think it is time to have a period – similar to the drop-off of progesterone that occurs at the end of a menstrual cycle -- triggering bleeding. If this occurs, try lowering the estrogen dose (if the patient is taking estrogen) and switch to topical progesterone.
 - Following topical application, progesterone levels are sustained throughout the day – without a drop-off. This more closely mimics ovarian release and also helps reduce the incidence of breakthrough bleeding
 - Oral Prometrium[®] can also cause nausea, a foggy head, and breast swelling. The reason for the breast swelling is that 1) short exposure of progesterone can actually cause estradiol to be more proliferative, and 2) progesterone when taken orally can be metabolized into estrogen.
 - Short exposure of progesterone leads to possible increased estrogenic effects, whereas the sustained activity of topical progesterone down regulates estrogen receptors.
 - A significant advantage of Prometrium[®] is that it is very sedating. In some situations, perimenopausal women may improve their quality of sleep by taking Prometrium[®] instead of using sleeping pills or antidepressants. Additionally, progesterone will not decrease libido, as most antidepressants will.

You have heard the Terminology - Here is what it means

Down regulation of estrogen receptors by progesterone: A rise in the level of progesterone causes a decrease in the number of active hormone receptors available for estrogen.

Up regulation of estrogen receptors by progesterone: A drop in the level of progesterone makes estrogen receptors more sensitive and receptive to the effects of estrogen.

A Collection of Notes about Cortisol

Stress (or distress) leads to increased cortisol levels which causes:

↑ Estrogen dominance

↑ Blood glucose and ↑ insulin resistance and ↑ abdominal weight (apple shape body)

↓ Progesterone activity

↓ Thyroid receptor activity (↓conversion of T4 → T3)

- Cortisol is secreted by the adrenal glands (tiny glands that sit on top of the kidneys) in response to stress (the adrenal glands release cortisol, adrenaline, and DHEA). Cortisol is the master stress hormone in the body. Cortisol's effect on the immune system is double edged: Acute stress causes cortisol to pump up the body's defense mechanism. Chronic stress, however, weakens the immune system and makes us more vulnerable to bacteria and viruses.
- Elevated cortisol makes you feel old before your time. Chronic stress and elevated cortisol leads to ↓ DHEA
- In times of high stress, the adrenals "steal" progesterone from women to make extra cortisol contributing to estrogen/progesterone imbalance.
- Highest levels of cortisol occur upon awakening and decrease throughout the day.
- Transdermal metformin is being used successfully in patients with elevated PM cortisol.
- Elevated PM cortisol causes sleep problems. Oral Progesterone may be beneficial in these women.
- Patients with low morning cortisol frequently complain about feeling tired in the afternoon.
- Elevated cortisol symptoms: osteoporosis (bone loss), muscle wasting, brain neuron atrophy, irritability, brain fog, feeling "burned-out", fatigue, low sex drive, weight gain at the waist ("apple" shape), insomnia, sleep apnea, metabolic syndrome (elevated insulin, high triglycerides, Low HDL, High LDL).
- Symptoms of adrenal fatigue (usually preceded by a period of prolonged stress or illness): fatigue, allergies, feel cold all the time, cannot get started in the morning, low sex drive, feel flat, feel burned out, depression, unstable blood sugars, too "wired" to fall asleep, difficult time relaxing. 80% of patients suffering from adrenal fatigue have low thyroid.
- Cortisol can increase estradiol formation in abdominal fat (occurs in men and women).
- Modestly elevated cortisol in chronic stress can increase Reverse T3 levels and decrease Free T3 levels.
- Adrenal Support includes: gentle exercise, avoid caffeine "pick-me-ups," supplement diet with B-complex and Vitamin C, drink plenty of water, take naps when needed, be open to love and laughter.
- Patients with severe stress in their lives should consider a 4-tube saliva collection to look at cortisol patterns throughout the day. These special cortisol collections kits are available through ZRT labs.

A Collection of Notes about DHEA

- Saliva testing has shown that patients with autoimmune diseases (Lupus, Rheumatoid Arthritis, and MS) have low levels of DHEA. Highest levels of DHEA occur in the morning.
- DHEA helps immune function and glucose handling. DHEA opposes the effects of cortisol.
- Oral DHEA can convert into testosterone or estradiol. Conversion is sometimes unpredictable – some women convert oral DHEA into testosterone, some men convert oral DHEA into estrogen. If you take oral DHEA, the best product is a slow release, micronized DHEA capsule.
- Topical administration of DHEA is approximately $1/5^{\text{th}}$ – $1/10^{\text{th}}$ of the oral dose
- Teens usually have higher DHEA concentrations, which causes a local conversion to testosterone in the skin that causes acne.
- Oral doses of DHEA for women are usually in the 5-15mg per day range
- In men, low DHEA correlates with hypertension and hyperinsulinemia

A Collection of Notes about Thyroid Balance

- Patients that are constantly feeling cold, chronically fatigued, frequently constipated, have brittle nails, and thinning hair, should have an extensive thyroid work-up
- To check thyroid function, first check your temperature for five consecutive days. The test is performed by placing a thermometer deep in the axilla (armpit) for 10 minutes. This needs to be done immediately upon awakening in the morning, before getting out of bed. Women should begin taking their temperature on the second day of menstruation, which is the time of the cycle that the temperature is the lowest. Typically the temperature is taken for five consecutive days and the results averaged.
- If the average temperature for the five days is below 97.0 degrees F, a complete thyroid panel should be done which includes TSH, Total T4, Total T3, Free T4, Free T3, Reverse T3, and TPO (thyroid peroxidase antibody) levels.
- There are an increasing number of patients who are presenting with “subclinical hypothyroidism” (normal - mildly elevated TSH, with normal T3 and T4 levels). It is estimated that 15 percent of women over the age of 60 have subclinical hypothyroidism. A free T3 level should always be part of a normal thyroid workup
- Subclinical hypothyroid is best treated with a low-dose of Natural Thyroid USP (Armour), which provides a mix of T4 and T3 hormone. The body converts T4 into T3, but there are many patients who can't convert T4 to T3 adequately. The usual starting dose of natural thyroid is 15mg daily. Sometimes natural thyroid is supplemented with a low-dose of slow release compounded T3 (7.5 mcg BID). Apothecary Options compounds a slow release version of Armour Thyroid which is very popular with patients. Slow release helps reduce the “afternoon crash” some thyroid patients experience.
- T4 replacement alone may be sub-optimal in many patients – despite a normalization of their TSH. Patients taking T4 who still have hypothyroid symptoms should have a more extensive thyroid workup.
- We all need adequate zinc, selenium, and chromium supplementation to convert T4 into T3
- T3 has a short biological half-life. Many clinicians recommend that Natural Thyroid or plain T3 be taken twice daily (_ dose in the morning, _ dose in the late afternoon/early evening) to compensate for T3's short half-life. Compounded, slow release versions of these products are beneficial to many patients because they provide more sustained levels of thyroid hormone and help mimic the natural thyroid release patterns in the body.
- Another advantage of slow release thyroid is that the gradual release of hormone in the body minimizes side effects that are sometimes seen with immediate-release thyroid including: heart palpitations, nervousness, feeling hot & sweaty, fine tremors, and clammy skin.
- The ovaries need T3 to be able to produce progesterone. Stress can decrease T3 levels, which in turn will decrease progesterone production.
- Often doctors check a TSH level to determine thyroid function. Even if the TSH level is normal, it just means that the brain is seeing adequate T3. There is no feedback mechanism for the rest of the body to tell the thyroid gland if it is getting enough T3. **Many patients with untreated hypothyroidism have “normal” TSH levels.**
- High cortisol due to stress causes T4 to shunt more to Reverse T3 (rT3). Reverse T3 is biologically inactive and levels tend to parallel those of T4 in normal subjects. Reverse T3 and T4 are observed to have low concentrations in hypothyroidism and elevated levels in hyperthyroidism. Patients with metabolic disorders tend to have a decreased conversion of T4 to T3 while conversion of T4 to rT3 is increased.
- Hypothyroidism is most common in women during the perimenopausal and postmenopausal years. Approximately 26% of women in or near menopause are diagnosed with hypothyroidism. When estrogen is not counterbalanced with progesterone, a predominance of estrogen can actually block the action of thyroid hormone at the cellular level.
- Modestly elevated cortisol in chronic stress can increase Reverse T3 levels and decrease Free T3 levels.
- Excessive estrogen supplementation has anti-T3 effects. Excess estrogen (especially orally administered estrogen) causes an increase in SHBG (sex hormone binding globulin) which can also bind to thyroid hormone.
- Low T3 can cause hirsutism, low progesterone, and fertility issues.
- Apothecary Options compounds affordable slow release versions of Thyroid USP (same as Armour), plain T3, plain T4, and T3/T4 combinations. Our patients who use slow release thyroid don't want to go back to immediate-release tablets.

A Collection of Notes on Testosterone

- **Testosterone Production in Women** - 0.25 - 2mg per day (average 0.5 - 1mg)
- **Testosterone Production in Men** - A normal male adult produces 4-7 mg of testosterone per day
- Women using natural testosterone to improve sex drive notice an increase in sexual thoughts and sex daydreams after 3-4 weeks of therapy.
- Women without much body hair and not much muscle development should start on a lower dose of testosterone (0.5-1mg day)
- Women with more body hair and who are more musculature can start out with higher doses of testosterone (1-2 mg/day) without noticing any side effects.
- Skin changes (oil or acne skin), aggressive moods, fine facial hair, and scalp hair loss are all indications that a woman is using too much testosterone. Either use less testosterone per dose or use it less frequently if these side effects occur.
- Women with androgen-induce alopecia can benefit from taking Saw Palmetto and L-lysine supplementation (L-Lysine dose = 500mg three times daily).
- Too much testosterone does not increase a woman's libido. In fact, too much testosterone can result in aggressive behavior, which is unrelated to sex drive, and may reduce sexual desire. Hormone balance with estrogen, progesterone, and testosterone is what really increases sex drive. You can become unbalanced with testosterone just as you can become unbalanced with estrogen and progesterone.
- Estrogen replacement (alone) can further suppress testosterone production in the menopausal woman.
- Surgical menopause reduces testosterone levels more dramatically than natural menopause.
- Testosterone supplementation works better when balanced with natural estrogen and progesterone.
- Testosterone inhibits fat accumulation, has bone building effects, is associated with improved spatial-temporal reasoning, and language fluency.
- Patients with Polycystic Ovarian Syndrome (POCS) have higher levels of testosterone than other women. A ramping progesterone protocol for these women works very well (days 1-7 Progesterone 20mg twice daily, days 8-20 Progesterone 30mg twice daily, days 21-28 Progesterone 40mg twice daily). Metformin 500mg topically once or twice daily mixed in an anhydrous gel formulation also works well. These patients should also take milk thistle approximately 300mg twice daily, and increase dietary fiber intake to reduce estrogen load.
- Highest levels of testosterone occur in the morning in men and women.
- Testosterone production is significantly reduced when women take birth control pills.
- Testosterone helps balance the effects of estrogen and helps balance the effects of cortisol.
- Women who have experienced chronic high stress levels may be more at risk of low testosterone after menopause. After menopause, testosterone comes from DHEA, and chronic stress can impair DHEA synthesis.
- Topical progesterone has been reported to increase testosterone levels due to conversion in the skin. This response depends more on the individual. Make sure that progesterone supplementation is therapeutic (i.e. 25mg/day). Higher doses may cause more problems.
- High cortisol and low T3 can all cause low testosterone.
- Women looking for a libido effect from testosterone should apply the cream vaginally about 4 hours prior to the desired effect. Applying it too late in the evening does not work.

Natural Protection against Estrogen Overload

By John Steven Foster, MD - Associate Director of the Center for Integrative Medicine at Thomas Jefferson University in Philadelphia.

We are living in the age of estrogen. The food supply is laden with traces of herbicides, pesticides, and petrochemical residues from plastics, all of which have estrogen-like, endocrine disrupting effects in animals and humans. These xenobiotics, or foreign biological substances, have been linked to abnormalities and cancers of human tissues that are hormone sensitive, including fibrocystic breast disease, breast cancer, cervical cancer and dysplasia, endometrial cancer, endometriosis and ovarian disease as well as prostatic hypertrophy and cancer.

How can we protect ourselves from these influences? Eating a whole food diet of organic or biodynamic foods, free of pesticides, is an important first step. Healthy water is the next. Municipal water supplies may be sources of many chemicals and water in plastic bottles can contain residues of polycarbonate plastics called phthalates, which are endocrine disrupters. It is important to drink only pure mineral water or water that has been treated by a reverse osmosis (RO) system.

Our bodies regulate and eliminate estrogens by the action of detoxifying enzymes in the liver. There are two pathways of estrogen oxidation and conversion, one of which converts it to a beneficial and non-toxic form 2-OH estrogen and another which converts it to the 16-OH estrogen form. The 16-OH form is carcinogenic and causes diseases of tissues that are responsive to hormones, including disorders and cancers of breast, uterus, cervix and prostate, and probably lung and colon. Xenoestrogens push the system toward the 16-OH pathway both directly and indirectly.

Cruciferous vegetables such as broccoli, cauliflower, kohlrabi, bok choy, Brussels sprouts and cabbage contain a substance called indole-3-carbinol (I3C) which is activated and liberated when the vegetables are crushed in a wet environment, that is, when they are chewed, chopped, or pounded. In the presence of stomach acid, I3C combines with itself to form DIM (di-indolyl methane). DIM induces certain P-450 enzymes in the liver to block the production of the toxic 16-OH estrogens and enhance the production of the beneficial 2-OH forms.

Studies have demonstrated that DIM reduces the incidence of fibrocystic breast disease, cervical dysplasia, endometriosis, and prostate enlargement. In fact, the 2-OH form is not only benign but also enhances the process of apoptosis, the spontaneous death of damaged and cancerous cells. DIM also acts as an active surveillance for cancer cells. This is very exciting and while there is much to learn and more to say, I can state with assurance that this phytonutrient may be one of the most important protective substances of this new century.

It is very important to eat cruciferous vegetables every day for protection against diseases that may be induced by exposure to environmental estrogens. As raw cruciferous vegetables contain goitrogens (chemicals that may induce goiter), it is best to eat them fermented, because fermentation neutralizes these thyroid-depressing substances. (Cooking also neutralizes the goitrogens, but also deactivates I3C.) In fact, low rates of breast cancer in Polish women have been attributed to their daily consumption of sauerkraut. (Science News 9/23/00)

The amount of vegetables needed to supply adequate DIM for full protection or as part of a program of cancer treatment is at least two pounds daily. Of course, it is not always practical or possible to eat such large amounts of pickled vegetables. Fortunately, DIM is available as a supplement. I recommend it to almost any patient over 40 and anyone with a family history of breast or uterine problems as well as cancer of the lung, colon, or prostate. I also add DIM to any hormone replacement therapy program for an added safety factor to prevent the above diseases. I have also used DIM successfully to treat PMS.

Non-Hormonal Options to Improve Hormone Balance

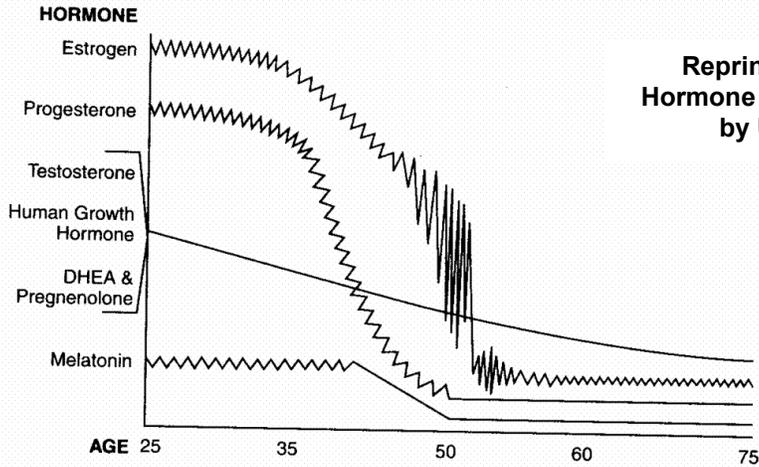
- Stress reduction (exercise, yoga, meditation, relaxation training)
- Weight loss through appropriate dietary changes – starvation is not the answer
- Weight training
- Dietary changes – reduction in hormone-fed animal products, reduction in refined carbohydrates. Supplement with adequate vitamins and minerals
- Eliminating vices (smoking, excessive alcohol and caffeine consumption)

BHRT Recommendations Based on Pocketbook -\$\$\$

Guess What? What is Best for your Body also happens to be Best for your Pocketbook!

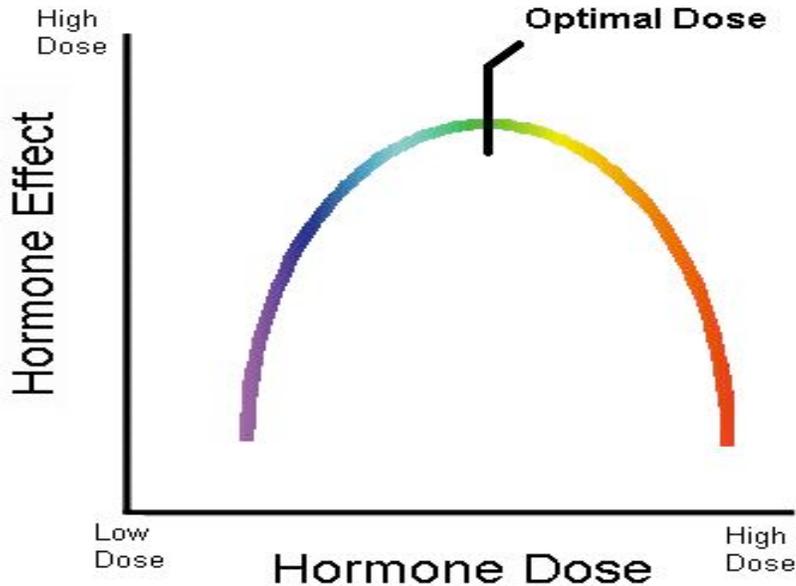
Menopausal Women or Women who have had a Hysterectomy				
Insurance? <u>Yes</u>	Have saliva testing done	Start on lowest dose of an <u>estradiol</u> patch, if needed. Available from your regular pharmacy. Do not use combination estrogen/ <u>progestin</u> patches	Use the patch every day as prescribed.	Cost – Whatever your co-pay for the estrogen patch plus <\$20 per month for our combination cream
		Start using progesterone + estriol (E3) +/- testosterone compounded cream	Use daily 25 days of the month. Skip 5 days/month Use vaginally 2-3 times per week in the morning.	
Insurance? <u>No</u>	Have saliva testing done	Start using a cream containing: low dose Bi-estrogen (if needed) + progesterone + testosterone	Use daily 25 days of the month. Skip 5 days/month Use vaginally 2-3 times per week in the morning	Cost < \$20 per month for our combination cream (estrogen, progesterone + testosterone)
Perimenopausal Women (ages 40-50)				
Insurance? <u>Yes</u>	Have saliva testing done	Start on lowest dose of an <u>estradiol</u> patch, if needed. Available from your regular pharmacy. Do not use combination estrogen/ <u>progestin</u> patches	Use the patch every day as prescribed	Cost – Whatever your co-pay for the estrogen patch is plus <\$20 per month for our combination cream
		Start using a cream containing progesterone + estriol (E3) +/- testosterone compounded cream	Use daily 25 days of the month. Skip 5 days/month Use vaginally 2-3 times per week in the morning.	
Insurance? <u>No</u>	Have saliva testing done	Start using a cream containing: low dose Bi-estrogen (if needed) + progesterone + testosterone	Use daily 25 days of the month. Skip 5 days/month Use vaginally 2-3 times per week in the morning	Cost < \$20 per month for our combination cream
Premenopausal Women (ages <40) – still menstruating				
Insurance? <u>Yes</u>	Have saliva testing done	Start using Prometrium® 100-200mg oil capsules (contains natural progesterone) Do not use if allergic to peanuts. Note: Pre-menopausal women usually don't require any supplemental estrogen.	Use daily at bedtime on days 15-26 of cycle.	Cost – Whatever your co-pay for the Prometrium® is.
Insurance? <u>No</u>	Have saliva testing done	Start using Natural Progesterone cream – compounded cream is better and more affordable	Use daily on days 15-26 of your cycle.	Cost < \$20 per month for natural progesterone cream

Reprinted from "Natural
Hormone Balance for Women"
by Uzzi Reiss, MD

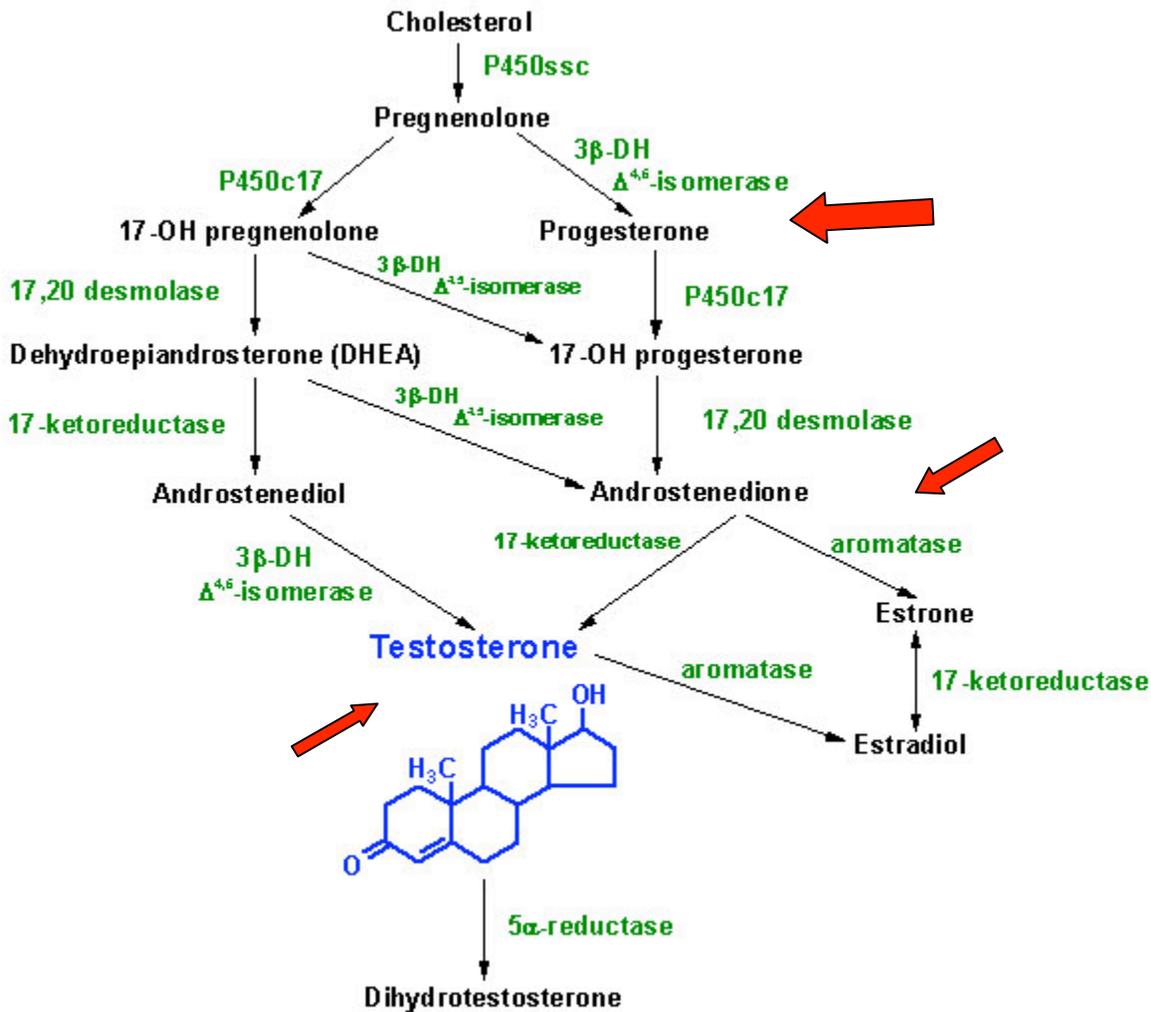


- Estrogen** – Significant fluctuations during peri-menopause. For women who still have ovaries, there is an approximate 40-50% decline in total estrogen by age 65. The biggest drop in estrogen occurs between ages 45-55
- Progesterone** – 75% loss from age 35-50 followed by further decline. Note: The reduction in progesterone production is much more dramatic than the drop-off in estrogen production
- Testosterone** – Steady drop in production as you age.

When it comes to Hormone Therapy -- More is Not Better Start low and go slow



In our bodies, hormones do not operate in isolation. Our hormones participate in a complex dance with all of our other hormones. Giving too much of one hormone can cause deficiencies in other hormones. Physiologic dosing of hormones will result in hormone balance with minimal adverse side effects. With hormones replacement, it is always best to "start low and go slow." And remember, if the initial good results wane, the starting dose was likely too high!



Sex Hormone Synthesis – Diagram #1

This diagram shows how our sex hormones all start out as cholesterol and then are converted in the body to the individual hormones. Pregnenolone is sometimes referred to as the “Mother Hormone” because all our sex hormones are ultimately derived from it.

The pathway further shows how progesterone is converted to androstenedione which is then converted in the body to either testosterone (via 17-ketoreductase enzyme) or to estrone and estradiol (via aromatase enzyme). Refer to the red arrows. How your body uses progesterone is individualized. Some women convert more progesterone to estrogen, and others convert more of it toward testosterone.

Note how oral DHEA can be metabolized either toward estrogen or toward testosterone. How a person is going to metabolize DHEA is not always predictable. Some women can metabolize oral DHEA more toward testosterone and experience androgen effects (facial hair, acne, or oily skin). Some men metabolize DHEA towards estrogen and develop breast tenderness. When supplementing with DHEA, always start at the lowest dose until you determine how your body is responding to it. Topical DHEA is not significantly metabolized.

The skin metabolizes hormones only to a small extent. Topical delivery avoids the first-pass metabolism in the liver and allows for a more sustained delivery of hormones.

Transdermal delivery produces therapeutic tissue concentrations of hormones at much lower doses (usually 1/5th – 1/10th of the oral dose is all that is needed to achieve the same results) – this is true for estrogen, progesterone, testosterone, and DHEA

How to get started On Bio-identical Hormone Replacement

1. All women (and men for that matter) should start by having baseline saliva testing done to establish baseline hormone levels and give an accurate picture of their current state of hormone balance or imbalance. Dosing based on symptoms alone is sometimes hit and miss – more art than science. **Saliva testing combined with symptom review is the most accurate way to get started.** Apothecary Options receives no financial compensation of any kind for recommending saliva testing. Saliva testing will be the best money you have ever spent on your health.
2. Fill out one of our consultation forms. **This service is FREE.** Go to our website www.apothecaryoptions.com and complete the form. If you do not have access to the internet, you can call us at 530-345-7979 and we will send a form in the mail. We must have a consultation form for you on file before we can make any specific recommendations.
3. Let our pharmacists review your saliva test results and medical history and give you a personalized recommendation. **This service is FREE.** Our pharmacists have extensive experience in the field of bio-identical hormone replacement. We take a conservative approach and recommend doses that work well with your own physiology.
4. After you receive our recommendation, discuss it with your prescriber.

Would You Like More Information? Internet Resources

✓ www.womeninbalance.org

Women in Balance is a national, non-profit organization comprised of women, doctors, health care professionals, national organizations and their members dedicated to supporting safe, effective and natural solutions for women's health issues in general and for the menopausal transition in particular. Women in Balance promotes safer, natural, and more effective approaches for alleviating menopausal symptoms and creating optimal health. The site contains very good scientific information regarding bio-identical hormone replacement.

✓ www.salivatest.com

ZRT Laboratory was established in 1998 and is independently owned and operated by David T. Zava Ph.D. a biochemist and breast cancer researcher. Dr. Zava developed saliva testing as a simple non-invasive, inexpensive way to identify hormone imbalances associated with diminished health and wellbeing. It is the mission of ZRT Laboratory to educate the public and health care professionals about the importance of Hormone Balance in maintaining optimal physical and mental wellbeing. This website is a great resource for men and women who would like more information on hormone balance, cancer resources, and help finding a prescriber in your area who is experienced in BHRT. ZRT laboratory has a 24-Hour Hormone Hotline (503-466-9166). You can listen to a variety of audiotapes on hormone balance and Bio-Identical Hormone Replacement.

✓ www.project-aware.org

Project Aware is a website by women, for women. The website offers objective and comprehensive health information, especially related to menopause, perimenopause, and postmenopause.

✓ www.hystersisters.com

HysterSisters Hysterectomy Information and Support website provides women with resources, information, discussions, and support for their hysterectomy needs. Specialty information: Hysterectomy Timeline Checkpoints, pre-op information, post-op information, hormone therapy options, cancer concerns, and more. HysterSisters is a "women to women" website. This website is a good resource for women who are contemplating a hysterectomy, as well as those who have already undergone the procedure.

HRT Bibliography

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