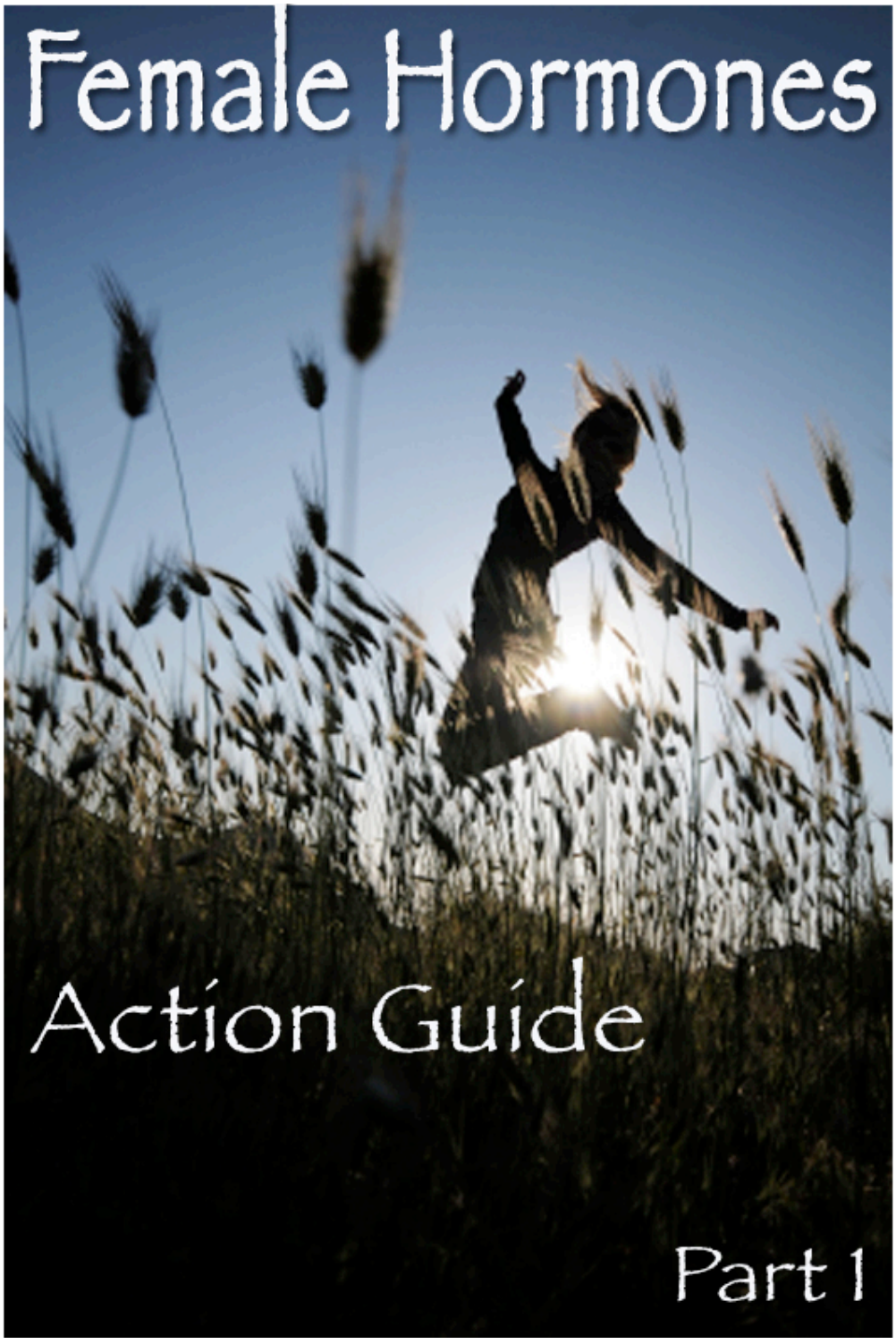

Female Hormones
Action Guide
Part 1

Your Step by Step Guide to Restoring Female Hormone Balance

Complete the Master Symptom Questionnaire to determine if your health symptoms are likely related to imbalances or deficiencies of the sex hormones, thyroid hormone or cortisol from the adrenal gland, poor intestinal / liver health, or chronic Candida (yeast) infection.

Hormone Basics

Hormones control just about everything in the body! They are responsible for growth, metabolism, immune function, healing and aging. They control sexual activity, mood, hunger and thirst. They prepare the body for puberty, mating, and parenting. And if that were not enough, they control the fight-or-flight response that allows us to perform superhuman feats.

Hormones are *chemical messengers* produced by various glands throughout the body. *Endocrine* glands secrete their hormones into the bloodstream to be carried throughout the body. *Exocrine* glands secrete there hormones into a duct or the surrounding tissue, thus tending to effect a more localized area.

The steps involved from hormone production to the intended effect include:

1. **Production**, **storage** and **release** by a hormone producing gland
2. **Transport** through the blood or tissue to intended cells
3. **Recognition** of the hormone by the target cell
4. **Relay** and **amplification** of the hormone signal into the target cell
5. **Elimination** of the hormone

Some hormones activate or stimulate the release of other hormones. Most have their effect by instructing the target cell to perform a specific task. There are three main types of hormones in the body, amines, peptides and steroids. *Amines* derive from amino-acids and include adrenalin and thyroid hormone. *Peptide* hormones are long chains of amino-acids and include insulin and growth hormone. The *steroid* hormones are all derived from cholesterol and make up most of the adrenal and the sex hormones.

Steroidogenic Pathway

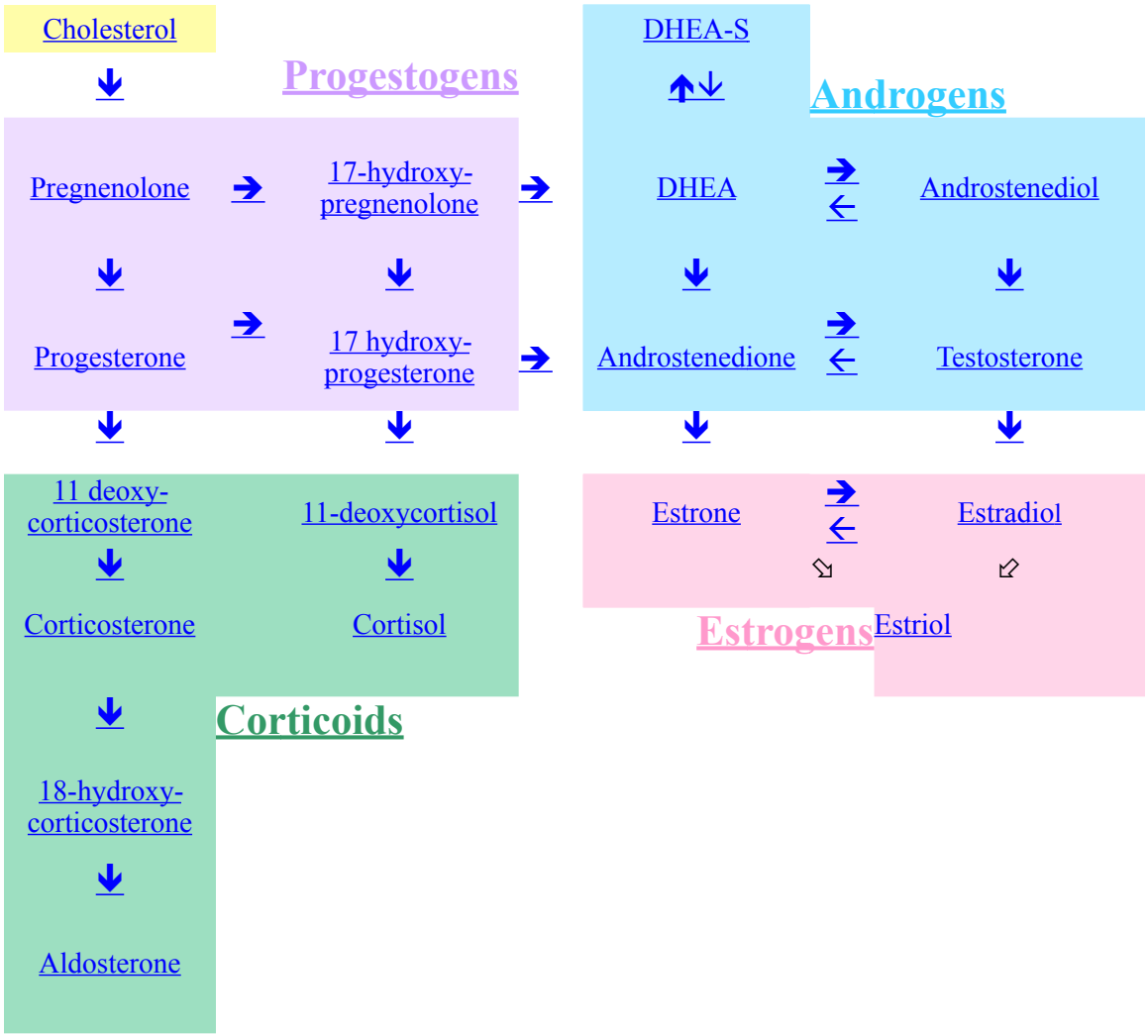


Diagram 1
Steroid Hormone Pathway

Hormone Control

The *pituitary* gland is the control center between the brain and the endocrine glands. A special part of the brain called the *hypothalamus* constantly monitors the condition of the body and the various hormone levels and sends chemical messages to the pituitary, encouraging it to either increase or decrease the pituitary hormones that control the endocrine glands. This system could be compared to a home heating system, in which the hypothalamus is the thermostat, the pituitary is the control switch, and the endocrine glands are the furnaces.

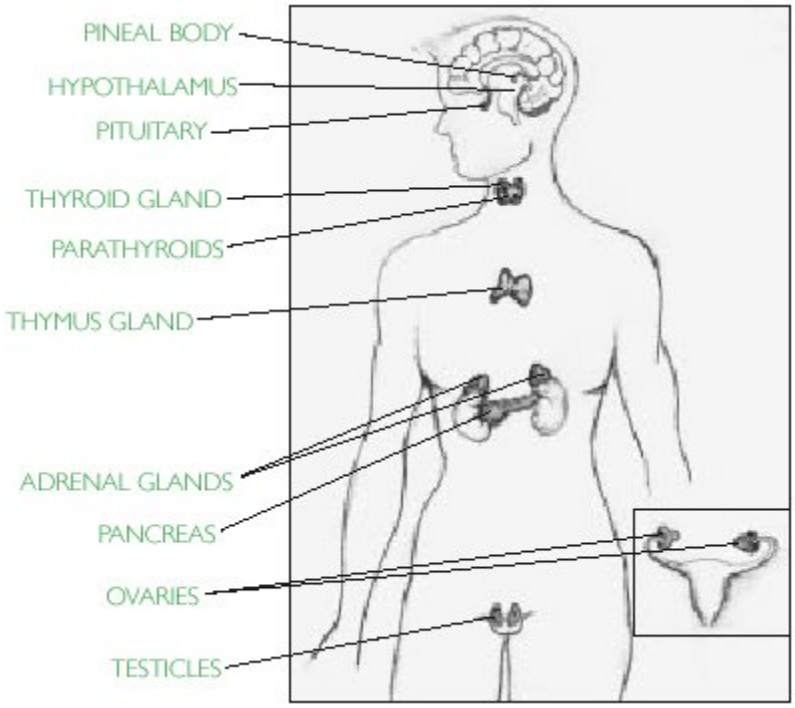


Diagram 2
Location of endocrine glands

Hormone production is controlled by a feedback mechanism. The target cells that make hormones as well as other glands that control the target cells will change hormone production based on the state of the body and circulating hormone levels. This provides a means to tightly regulate the amount of hormones.

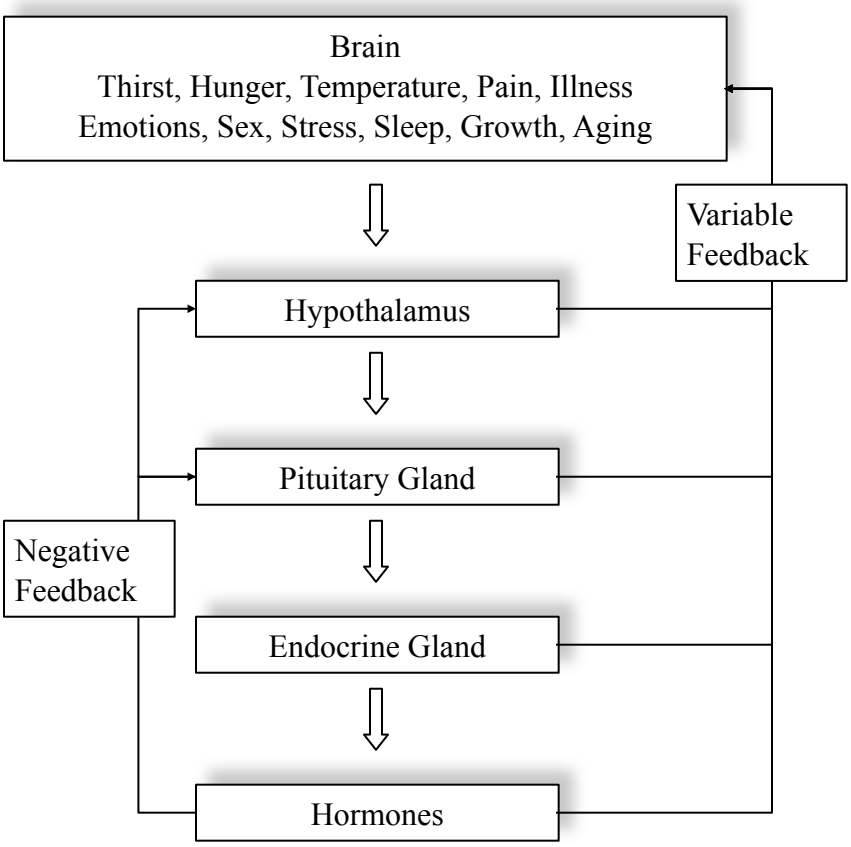


Diagram 3
Hypothalamus-Pituitary-Endocrine gland axis

Hormone deficiencies affect every cell in the body and result in degenerative changes and aging. A predictable decrease in the production of some hormones begins in middle age and continues until old age.

Hormone imbalances can occur due to lifestyle or pathological conditions that impact the production of hormones. This can mean hormone levels going up or down.

Factors that decrease hormone production include:

- Chronic Stress
- Poor sleep
- Poor nutrition
- Excess sugar, alcohol or caffeine
- Impaired intestinal health
- Aging

Factors that increase hormone production include:

- Deep restful sleep
- Proper nutrition
- Exercise
- Herbals
- Targeted supplements
- Glandular extracts
- Hormone replacement

Hormone imbalances also occur as some hormones normally decline with aging (such as estrogen dominance due to progesterone deficiency).

Hormones interact in a wonderful and complex manner, such that changes in one hormone system will have an affect on other hormones. Much like a symphony missing certain instruments, if the endocrine system is missing certain hormones then the whole body suffers.

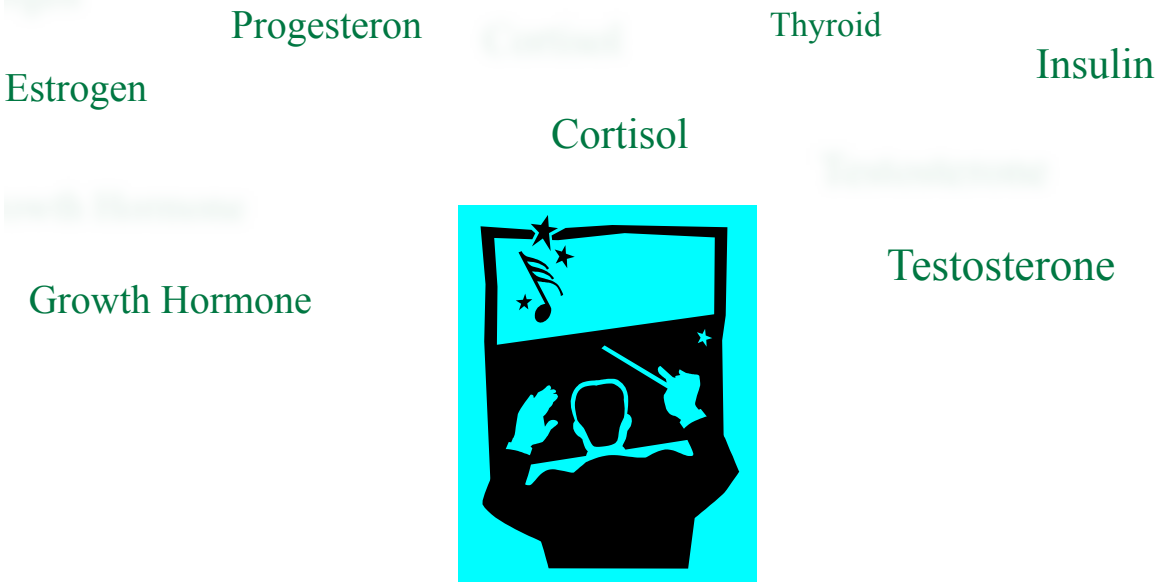


Diagram 4
The Symphony of Hormones

Hormone Replacement

Hormone replacement is an aggressive, proactive process designed to prevent disease and maintain quality of life.

As hormone production declines there are inevitable consequences for the body. The degenerative diseases of aging are due in part to the decline in hormone levels. Expecting the human body to operate smoothly without hormones is much like expecting our automobile to just keep running well without oil – and by the time the red light comes on it is too late! In the same manner, humans should keep their hormones at optimum levels in order to get the best performance from the body.

The types of hormones used for replacement should only be bioidentical and replaced in a physiologic manner and dose. *Bioidentical* simply means identical to our biology – the chemical molecular structure is exactly the same as that in nature. Many of the side effects and risks of hormone replacement is minimized or erased completely by using only bioidentical hormones. Nature is very, very specific, and making a drug that is similar enough to stimulate a hormone receptor, yet not bioidentical, is asking for trouble.

The following program will cover specific actions of the various sex hormones, what types of problems can occur when those hormones are out of balance or deficient, and what can be done to fix the problem. Because of the overlap in symptoms associated with hormone imbalances and the complex symphony that the endocrine system represents it is important to study each of the hormones.

If your initial Master Hormone Questionnaire points to thyroid or cortisol problems then it is often best to address these prior to working on sex hormones. Restoring intestinal health, removing food allergens, improving liver health, and treating chronic infections such as Candida are all important areas to consider prior to starting sex hormone replacement.

Like a great conductor making a symphony sound glorious, identifying and correcting hormone imbalances requires patience and diligence, but the reward of a healthy hormone system is the backbone of great health!

Step 1
Must know basics
Getting started on your journey to hormone balance

Learn the basics of what sex hormones do and how they affect you. Find out:

- What estrogen, progesterone and testosterone actually do
- How sex hormones control the menstrual cycle
- What happens with your hormones and your body at menopause

Estrogen is the main female hormone. It "feminizes" the body, developing the breasts and hips. It is the hormone that makes women sensitive, intuitive and sensuous. In general, estrogen stimulates the body, while progesterone balances that stimulation. Think of estrogen and progesterone as "sisters" that complement and sometimes antagonize one another. If estrogen is the gas pedal, then progesterone is the brake.

Estrogen Basics

Estrogen is made primarily from the ovary until menopause, then the adrenal gland and fat cells continue to make a small amount. There are three main estrogens in the body, **estrone (E1), estradiol (E2) and estriol (E3)**. E2 is the most potent and the most physiologically active. E1 is considered cancer promoting and is usually not prescribed. E3 is considered a weak estrogen but has been shown to have anti-cancer properties.

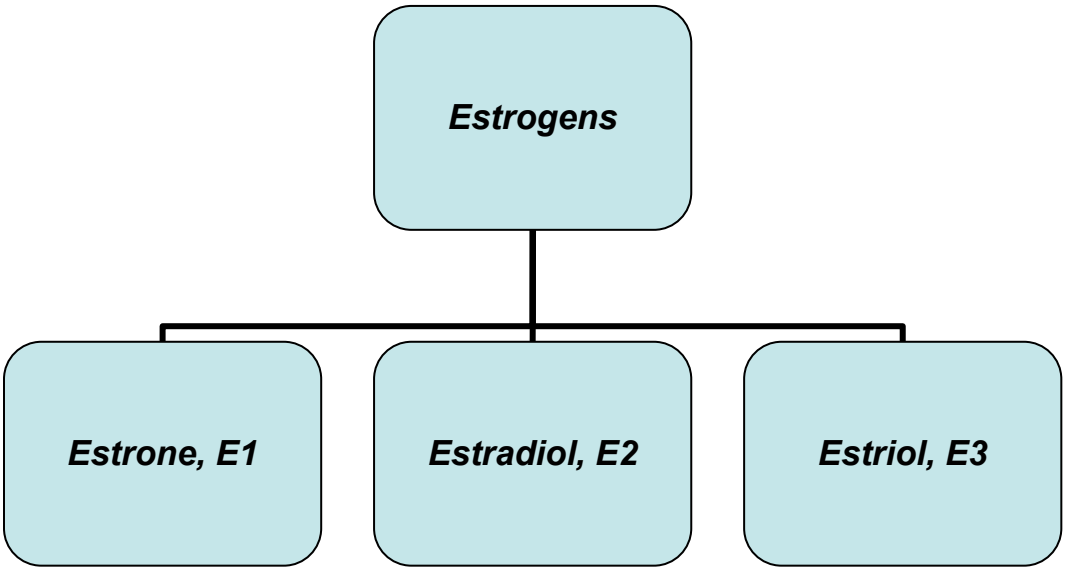


Diagram 5

Estrogens E1, E2, E3

Prior to menopause E3 is about 80% of a woman's estrogen – which is a good thing since E3 is a weak, cancer preventing estrogen. E1 is only 10-20% of circulating estrogen prior to menopause. It is likely that E3, like other weak, friendly estrogenic chemicals (e.g. soy) binds to estrogen receptors and blocks other more aggressive estrogens from binding and exerting their cancer promoting effects. (see estrogen receptors)

After menopause, all three estrogen levels decline, but the ratio of E3 to E1 reverses. Now the E1 is about 80% of circulating estrogen and the friendly E3 is only 10-20%. It is not known for certain, but this shifting ratio may have bearing on the increased breast cancer incidence *after* menopause.

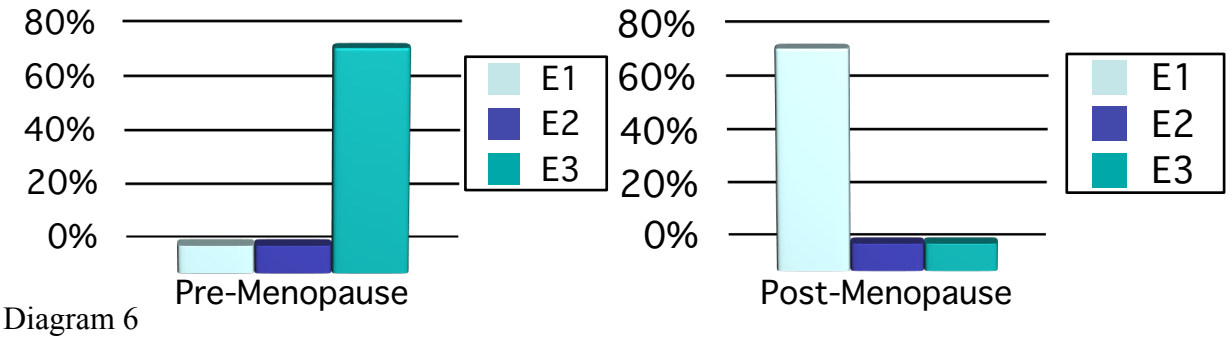


Diagram 6
Estrogen ratios before and after menopause

Below is a list of the functions and actions of estradiol:

- **Uterus** – Creates normal growth of the endometrium (lining) of the uterus. Excessive estradiol, or estradiol not opposed by progesterone, can increase the risk of developing endometrial cancer.
- **Vagina** - Promotes vaginal lubrication and thickening of vaginal wall
- **Urinary Tract**- Promotes bladder tone thereby preventing symptoms of stress incontinence.
- **Skin** - Has a positive effect on skin thickness, skin collagen, water content, skin softness and blood flow to the skin.
- **Breasts** - Helps maintain the size and density of breast tissue, though *excess* amounts increase risk of some forms of breast cancer or cause breast pain.
- **Bone** – Slows bone loss by decreasing the development and the activity of bone clearing osteoclast cells. It also increases the bone building ability of osteoblast cells directly.
- **Heart** – Lowers total and LDL (bad) cholesterol levels while increasing HDL (good) cholesterol. Also causes a reduction in lipoprotein (a) which results in a significant reduction in the risk of developing heart disease.

- **Blood Sugar & Insulin Levels** - Improves blood sugar metabolism and decreases risk of developing hyperinsulinemia. Estradiol promotes increases in the uptake of glucose by muscle cells.
- **Brain, Mood & Memory** - Can significantly improve or alleviate depression in postmenopausal women. It is needed for normal function of neurotransmitters that affect mood and memory.
- **Libido** - Can directly increase sexual desire, interest, responsiveness and sexual satisfaction.

Progesterone Basics

Progesterone is produced by the ovaries and adrenal glands and plays an essential role in pregnancy. Progesterone prepares the uterus for implantation of the fertilized egg and then continues to secure the pregnancy. Progesterone also works to balance the effects of estrogen.

Below is a list of the functions and actions of progesterone:

- **Uterus** – Prevents the development of endometrial cancer and helps prevent or decrease dysfunctional uterine bleeding. Progesterone may help decrease uterine contractions, cramping and pain.
- **Vagina & Urinary Tract** – Excess progesterone may counteract the beneficial effects of estrogen in maintaining urinary control and preventing vaginal dryness.
- **Skin** – Progesterone promotes increased blood flow to the skin resulting in an improved ability to sweat and loose extra heat through the skin. Progesterone can also raise body temperature, enhancing the ability to tolerate cold.
- **Breasts** – Progesterone protects the breasts from the normal stimulation of estrogen. Progesterone deficiency may play a role in the development of breast cancer; however, progesterone *excess* may also play a role in proliferation of some progesterone receptor forms of breast cancer.
- **Bones** – Progesterone has a stimulating effect on the bone building osteoblasts resulting in increased bone building activity. This is due to direct stimulation of the progesterone receptors in osteoblasts as well as increased secretion of growth factors by the bone cells exposed to progesterone. The most positive effect is seen when estrogen and progesterone are used in combination.
- **Heart** – May cause a significant lowering of blood pressure in postmenopausal women with mild to moderate high blood pressure, possibly due to the vasodilating effect of progesterone.
- **Blood Sugar & Insulin** – *Excess* progesterone can cause a decrease in insulin sensitivity having an effect on blood sugar (elevation) that is similar to glucocorticoids (steroids). This interference with the action of insulin can interfere with normal glucose uptake and cause insulin resistance.

- **Brain, Mood & Memory** – Progesterone and its metabolites result in increased relaxation and reduced anxiety in a way that is similar to the benzodiazepines (e.g. Valium or Xanax) by its direct effect on neurotransmitter receptors called Gamma-Amino Butyric Acid type A (GABAA) receptors. When progesterone levels drop, a woman can experience withdrawals similar to that seen with benzodiazepines, barbiturates and alcohol. This is one cause of post-partum depression. Progesterone also has a protective, stimulating effect on breathing patterns during sleep, resulting in decreased incidence of sleep apnea. It has also been associated with an increase in appetite and food intake.
- **Libido** – *Excess* may diminish libido due to progesterone's counteracting effects on estrogen and testosterone.

Testosterone Basics

The daily production of testosterone in women is 20-30 times less that of men. Despite the difference in production, testosterone is just as important in women as in men. The ovaries and the adrenal glands produce half of women's testosterone; the other half comes from "conversion" of steroid hormones, such as DHEA, to testosterone. Testosterone levels decline with age, usually beginning around age 40 in women.

Below is a list of positive actions of testosterone in women:

- Improvement of mood and assertiveness
- Reduction of depression and anxiety
- Improved bone density
- Improved muscle size and strength
- Enhancement of sex drive and sexual sensitivity
- May protect against atherosclerosis

The Menstrual Cycle

A woman's menstrual cycle is typically 28 days, with day 1 being designated as the first day menses begins. Estrogen and progesterone are at there lowest levels during menses.

Under the influence FSH (follicle stimulating hormone) from the pituitary the estrogen level starts increasing to rebuild the *endometrium* (lining of the uterus), with estrogen reaching its peak level around day 12. This day 1 to day 14 growth phase of the endometrium is called the *proliferative* phase.

A few days later, around day 14, *ovulation* (release of egg from ovary) occurs, under the influence of LH (lutenizing hormone) from the pituitary. Progesterone levels now begin

to increase, as progesterone is made primarily from corpus luteum (unfertilized egg). This stops estrogens effect on thickening the endometrium and causes it to mature in preparation for pregnancy. Day 14 to day 28 is designated the *secretory* phase, or the *luteal* phase.

If the egg is not fertilized then the estrogen and progesterone levels plummet around day 26-27 causing the rapid, organized sloughing of the endometrium, starting menses and another 28 day cycle.

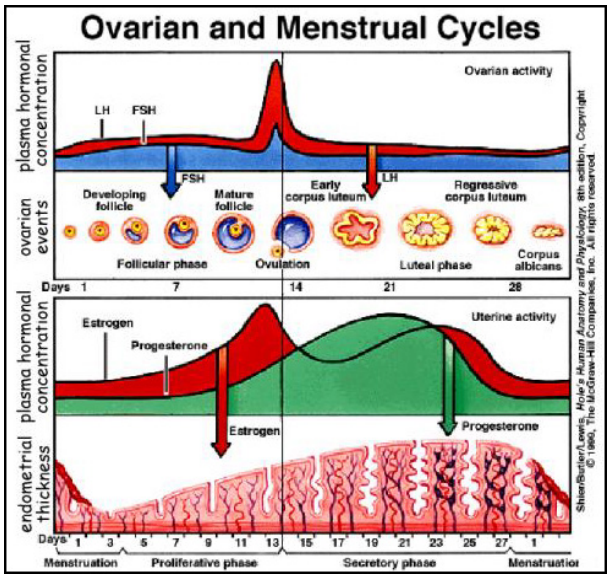


Diagram 7
Menstrual cycle

If the delicate balance between estrogen and progesterone is not just right then problems with the menstrual cycle occur.

Menopause

Menopause is by definition the "end of monthly cycles" and signals the end of fertility for women. The *peri-menopause* is the "time around menopause" or the time leading up to and after menopause, which may be a few years or even decades. During the peri-menopause the complex balance of estrogen and progesterone is shifting, which can lead to disruption in the normal physical and mental state of women, particularly as it relates to the patterns of the menstrual cycle. (see case scenarios)

"Menopausal symptoms" such as hot flashes, night sweats and mood swings are not from hormone deficiency, per se, rather from hormone withdrawal, particularly estrogen. On average these symptoms last a few years, with some women having no withdrawal symptoms at all, and others suffering from them for many years. As ovarian production of estrogen begins to decrease, the pituitary increases the output of FSH and LH in an attempt to keep up production. Each time a pulse of FSH and LH surge it is associated with a hot flash. About half the normal activity of the pituitary happens between midnight and 4 am, which is why hot flashes cluster at night (night sweats). Eventually the pituitary "gives up the battle" and quits trying to stimulate estrogen production, and with that the menopausal symptoms abate.

On average, menopause occurs about age 52, but may happen in the early 40s or even late 50s. The peri-menopause may also start as early as the late 30s or continue into the 60s.

After a hysterectomy, if the ovaries remain, of course menses will stop, and much of the time the hormone production from the ovaries will continue until a natural age. On the other hand, the ovaries *may* shut down within weeks after a hysterectomy. If a woman needs a hysterectomy at an early age, say in the 20s, then it seems reasonable to leave the ovaries as they are likely to produce hormones naturally for many years. If a woman is in her 40s when she needs a hysterectomy, then it starts making sense to remove the ovaries as well (mostly to avoid the possibility of ovarian cancer) since the ovaries are going to shut down hormone production soon anyway.

Step 2
Discover which hormone imbalance you may have

Let's determine which category you are in so you know where to begin

- How to determine which hormone is deficient
- Are you Premenopausal?
- Have you arrived at Menopause?
- Do you have a hormone imbalance that is not related to menopause?

Symptoms and Diseases Associated with Estrogen and Progesterone Deficiency

By understanding the beneficial, intended effects of estrogen and progesterone it should make sense that a deficiency of either hormone will lead to undesirable effects.

Symptoms of Estrogen Deficiency

- Hot flushes and night sweats
- Small, "droopy" breasts
- Vaginal dryness and itching
- Low or absent menstrual cycles
- Urinary incontinence, increased bladder infections
- Pale and dry skin
- Poor libido (sex drive)
- Depression and fatigue
- Poor memory

Symptoms of Progesterone Deficiency

Most signs of progesterone deficiency are in fact signs of estrogen excess.

- Painful, swollen and/or cystic breasts
- Heavy menstrual cycles
- Increased pre-menstrual symptoms
- Endometrial hyperplasia and uterine fibroids
- Muscle and nerve tenseness
- Increased abdominal fat
- "Reddish" skin
- Increased irritability and anxiety
- Insomnia
- Increased aggressiveness, especially during "PMS"

Symptoms of Testosterone Deficiency in Women:

- Decreased or absent: libido, clitoris sensitivity and/or orgasm
- Vaginal itching
- Painful intercourse
- Reduced muscle strength
- Joint pains
- Dry skin
- Depression
- Excessive anxiety and worrying
- Excessive emotions
- Inability to deal with stressful situations

The following diseases are linked to deficiencies in estrogen and progesterone:

- Osteoporosis
- Heart disease
- Stroke
- Alzheimer's
- Cognitive decline
- Colon cancer
- Tooth loss
- Macular degeneration

Clinical Scenarios

It seems no two women experience hormone imbalances just alike. Nevertheless there are several common patterns that we observe. Recognizing these patterns and getting treatment is a blessing for health *and* peace of mind for many women.

"Estrogen Dominance"

Jeanie was 45 years old and losing control of her life. She used to be active, healthy, and in her words "normal". In her early 40s she started having problems with heavy painful menstrual cycles, which had progressed to the point that her gynecologist was recommending she have a hysterectomy. Anxiety and insomnia were her new worst enemies. She was so tired from poor sleep she could hardly function in the daytime. Her anxiety and impatience was straining her job and her marriage. She was put on birth control pills to control her cycles, which only made other symptoms worse. In her words, she was "like a train about to derail".

Aside from the mental torment, this type of hormone imbalance puts women like Jeanie at risk for estrogen dominant physical problems such as uterine fibroids, which can cause excess bleeding and cramping, and the all too frequent outcome is a hysterectomy. Breast cysts, adenomas, and abnormal mammograms become the norm for many women like Jeanie. Little did she know she was also at increased risk of breast cancer and quickly losing bone density.

Jeanie's story is very common and we treat many patients like her. With the right hormone supplementation the mental symptoms such as insomnia, anxiety, irritability and impatience can usually be gone right away. In addition, the physical symptoms of estrogen dominance can usually be eliminated within the first few menstrual cycles. As she said to me, Jeanie now "has her life back and feels normal again". Her anxiety and insomnia cleared up right away, and she is thankful to be able to cancel her planned hysterectomy. Her husband and family, as well as boss and co-workers, are glad to have her back!

Comments: Progesterone is the first to go in many women, starting in the late 30s or early 40s, and becoming more common as they get closer to menopause. The resulting estrogen is left unbalanced and estrogen dominance ensues. By simply cycling progesterone several weeks during the 28 day cycle the estrogen dominance is eliminated.

"Menopause Blues"

At age 52, about a year before her last menstrual cycle, Pam started having hot flashes and night sweats. For the first time in her life she was not sleeping well. She had always been healthy, ate well and exercised, and did not like to take medications. When she talked to her doctor about her symptoms, she said "not to worry unless the symptoms got worse" and prescribed a medication to help her sleep. A year later she had gained 20 pounds, mostly around her belly, and for the first time in her life exercise was becoming a chore. She not only continued her excellent habits but actually increased her exercise routines in a failing attempt to control her weight. At this point she also noted her previously healthy sex drive had disappeared, much to her and her husband's disappointment. Furthermore, Pam was suffering from mental changes, with difficulty concentrating and a depressed mood. Now she was really beginning to panic.

Pam was very motivated and had read several books about menopause and hormone replacement. She asked her doctor for help, was told "hormones cause cancer" and prescribed an anti-depressant. So now she was on a sleeping pill and asked to start another medication – she did not approve of this state of affairs! That is when Pam found our clinic.

The first thing Pam found at our clinic was education. We strive to clarify the myths and misunderstandings regarding hormone replacement so that our patients feel informed and confident in their treatments. Pam was started on a bioidentical hormone replacement protocol. She was educated in detail about each of the ovarian hormones – estrogen, progesterone, and testosterone. She was comfortable making minor adjustments to her hormone replacement until it was fine-tuned to just the right blend for her.

Within a month of seeing us Pam was sleeping well without medication and was feeling normal again, with a "sharp mind and great mood". After a few months her sex drive and motivation to exercise had returned. The weight she had gained quickly came off with her usual excellent diet and exercise habits.

Pam is thrilled to be in control of her body and mind again. Her muscle tone is good and her sex life "great"! She is also happy to know that despite the hysterical media and mistaken medical advice she is not at increased risk of breast cancer, and in fact has markedly decreased her risk of getting heart disease, dementia or osteoporosis.

"Post-Menopause Surprise"

Ruth went through menopause without a single withdrawal symptom - at age 50 she simply stopped having menstrual cycles. By age 55 things were starting to look a little different. She had slowly accumulated 15 lbs of weight, which was the first time in her life she weighed more than she did right of high school. More disconcerting to her though was her loss of muscle mass and stamina. She enjoyed trail running and cycling and was not at all able to keep her usual pace. During her annual check up her doctor ordered a routine bone density scan which showed she had osteopenia (bone loss) and was close to osteoporosis (brittle bone). She was flabbergasted that despite good health habits and the usual calcium supplementation for bone health she was now in trouble!

She was started on a bisphosphonate medication (e.g. boniva, fosamax) and took that for a few months. But after learning about the potential side effects and conflicting studies on efficacy she was disconcerted with the medication.

Ruth had a hormone deficient disease, loss of bone or osteopenia. She also had vaginal dryness, low libido, loss of muscle mass, and increased body fat – all signs of hormone deficiency. Before starting HRT we analyzed her cardiac risk factors and did a plaque assessment. We found she was also starting to make plaque in her arteries, another condition associated with hormone decline.

Comments: Ruth is a dramatic example of the difference between hormone withdrawal and deficiency. She did not have *any* symptoms of withdrawal, such as night sweats, hot flashes or mood swings, yet within a short time was showing signs of hormone deficiency. The physical symptoms were evident to her, but the physical diseases were

not. Luckily she was able to turn everything around. Her artery health was addressed first with targeted supplements that improved her risk factors and stabilized the plaque. Then we were able to safely start BHRT and within a short time her bone markers were looking better.

Other Conditions of Sex Hormone Imbalance

There are conditions that lead to sex hormone imbalances other than the natural decline in hormones leading up to menopause. Recognizing these situations is the first step to getting proper treatment. Many times simply replacing the sex hormone is not the ultimate treatment as the sex hormone imbalance is due to an underlying problem. It is best to seek out the root cause of the imbalance and target it directly.

Estrogen Dominance

Many women suffer from estrogen dominance throughout their adult life either from exposure to environmental estrogens, poor estrogen metabolism and clearance, or lack of progesterone. Eliminating xenoestrogens (see section below) is an important first step in addressing estrogen dominance. Next we consider gut and liver health – the beneficial bacteria in the intestine play a role in preparing estrogens for future elimination in the liver. Insuring proper liver detoxification is the next step. (see my guide for gut health and detox for detailed treatment suggestions). The next conditions listed below are causes for low progesterone production.

Polycystic Ovarian Syndrome (hormone confusion syndrome)

Polycystic ovarian syndrome (PCOS) is a condition where women do not ovulate regularly and make excess testosterone hormone. The result is that women with PCOS typically have only 3-4 menstrual cycles per year and may have difficulty getting pregnant. The elevated testosterone results in excess body hair and/or acne.

The underlying cause of PCOS is usually due to insulin resistance, similar to diabetes, and should be treated as such. Many women simply get started on a birth control pill to force regular menstrual cycles, which does nothing to treat the real underlying cause!

Obesity often results from the insulin resistance found with PCOS. Treating the condition with proper diet and exercise, weight loss, and supplements or medications to help insulin work better will usually result in a cure. Until the condition is cured, and in cases where a cure is not achieved, progesterone cycling is the preferred treatment.

Premature Ovarian Failure

Incorrectly called “premature menopause” the condition of premature ovarian failure (POF) is truly a unique process. Early menopause is where the ovaries run out of eggs and shut down earlier than the average age of 52. POF is a little understood process whereby the ovary shuts down long before running out of eggs. It is associated with other autoimmune diseases and many feel POF is an autoimmune disease.

Women with POF are at great risk for hormone deficient diseases such as osteoporosis and heart disease and need to consider BHRT right away. About 1 in 10 women with POF will eventually get pregnant. We are finding that by addressing the potential “triggers” for autoimmune diseases in general we are able to restore normal ovarian function for some women. (see my guide to reversing autoimmune diseases)

Luteal Phase Defects

Luteal phase deficiency (LPD) of progesterone occurs when women don’t ovulate normally, don’t produce a normal egg (corpus luteum), or don’t make enough progesterone. The resulting menstrual cycle is often shortened and estrogen dominant. The time after ovulation until menses (the luteal phase) is usually two weeks in duration. Women with LPD will typically have shortened luteal phase time which can be measured by basal body temperature charting. Treatment of this condition should include ruling out hormone disorders of low thyroid or high prolactin. This condition is best managed by a specialist in reproductive endocrinology.

Low Thyroid and Low Adrenal

The ovary needs proper amounts of thyroid in order to ovulate and make enough progesterone. The adrenal hormone, cortisol, has an influence on ovarian function as well. In patients with estrogen dominant menstrual cycles it is important to screen for underlying thyroid and cortisol disorders. Use my master hormone questionnaire to screen your symptoms for these hormone disorders. If indicated see my guides for restoring thyroid or adrenal hormones.

Step 3
Time for Lab Testing

Tips for knowing what tests to ask for:

- Guidance on getting the right tests
- Do you even need lab testing?
- Guidance on getting the right *type* of testing
- Confirmation of what category you are in
- Rule out other illness that may influence your sex hormones
- Rule out other illness that may cause similar symptoms

Testing

Determining hormone levels in the body is an important part of safe and effective HRT. I am frequently asked "when do we test" and the answer varies depending on the particular patient scenario. Often, no initial testing is necessary as the clinical situation is obvious. We always test hormone levels after starting HRT in order to insure balance and adequate levels.

I stress to my patients, and to you, that understanding the different phases of hormone decline and types of hormone imbalances between estrogen and progesterone is of the utmost importance. No test can completely replace understanding the physiology of what is happening to your body and no test can tell you exactly how much hormone to take.

At this point in your reading, you are likely able to determine which category of hormone imbalance you have and what treatment is likely needed.

Testing for estrogen and progesterone may be done by serum, saliva or 24 hour urine collection. There are advantages and disadvantages to each method.

Serum testing of estrogen and progesterone has the advantage of being easy to obtain, provides quick results, and is relatively inexpensive. Serum testing offers relatively accurate values with well-established reference ranges. One disadvantage is that serum testing measures the "total" hormone level which includes the free and unbound portions. Only the "free" portion is bioavailable and active so measuring the total hormone level in the blood is subject to some misrepresentation of what portion is actually free. The "free" hormone levels are calculated from the total serum levels. Only estradiol, estrone and progesterone are available in serum testing, while estriol needs to be measured by saliva or urinary testing.

Saliva testing has become quite popular in recent years and has the advantage of being patient controlled and inexpensive, especially when obtaining hormone levels over several days such as when checking throughout the menstrual cycle. Hormone levels in saliva are representative of those in tissue, which is supposedly more accurate than serum testing as it measures only the "free" or unbound and active portion of the hormone, plus the tissue is where the hormone has its effects. Others argue that the hormones may accumulate in the saliva and give a false impression of elevated hormone levels leading to under-dosing of the hormone.

Serum and saliva both have the disadvantage of representing only a "snapshot" of the hormone level at the time it was sampled, and hormone levels may fluctuate greatly over the course of a day.

Urine collection over 24 hours provides the most accurate, comprehensive and quantitative measurement of estrogens and progesterone.

I have used serum testing for estradiol and progesterone for over a decade with thousands of patients and it has proven reliable in the clinical setting. I also use serum testing for estrone metabolite testing. After HRT is being taken a 24 hour urine test is appropriate to measure all the estrogens, progesterone, the estriol / estradiol ratio, and estrogen metabolites.

When testing hormone levels it is important to take your hormones the day of the lab test and within a specified time-frame. When taking sublingual tablets I request testing 4-6 hours later. With topical creams I request testing 8-10 hours later.

Routine Testing Scenarios

Use my master symptom questionnaire to screen for suspicion of other hormone disorders that may involve thyroid or cortisol and consider advanced testing. Intestine and liver health are also very important considerations and these can be tested with serum and stool tests.

If you are still menstruating then the best time to check the ovarian hormone levels is about 1 week prior to the next expected start of menses. In a 28 day cycle, the hormones are at their peak around day 21. There is not much point in checking estrogen and progesterone during menses as they are expected to be fairly low at that time. Sometimes your doctor may want hormone levels during menses or other non-peak times for a specific reason.

After menopause or in conditions where there is not normal menstrual cycling the hormones can be checked anytime.

I recommend checking estriol / estradiol ratios and estrone metabolism, as well as all ovarian hormone levels, within a few months of starting HRT.

Without a doctor's order you can obtain serum testing through several companies, including Life Extension (www.lef.org)

With a doctor's order, you can obtain serum testing through routine labs. Saliva testing and 24 hour urine testing is widely available and usually requires a doctor's order.

The following labs offer saliva or urinary testing, or both: www.genovadiagnostics.com, www.meridianvalleylab.com, www.labrix.com, www.zrtlab.com.

We have used all these labs and found them all to be good, reputable labs, with very helpful staff available to help interpret results.

Step 4

Getting Ready for Treatment

Cut through the medical myths and media hysteria surrounding HRT

- Learn about the real risks and benefits of HRT
- Learn which synthetic hormone "look-alikes" to avoid
- Learn why bioidentical HRT is truly safer and more effective

The Science of Bioidentical Hormone Replacement Therapy (BHRT)

Mixed messages, myths and misinformation are what most women have encountered when in comes to hormone replacement therapy (HRT). From the media hysterics to the medical mantra women have been left confused and abandoned. Seeking to do the right thing with their health many women have been sent down a spiraling course of medications that simply treat one symptom after another in a vain attempt to change the course of hormone decline. Interest in HRT is at an all time high and a few interesting trends are noted below.

Reasons women *don't* start HRT:

- HRT perceived as unnecessary
- Prefer to not take medications
- Fear of side effects
- Confusion over scientific information
- View menopause as "natural" event

Reasons women *do* start HRT:

- Osteoporosis prevention
- Relief of menopausal symptoms (esp. flushing)

Reasons women *quit* taking HRT:

- Side effects of bloating, breast tenderness, irregular bleeding
- Weight-gain
- Fear of cancer
- Physician recommendation

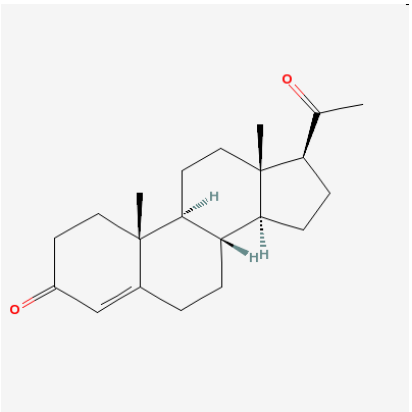
The majority of these side effects are due to the synthetic progestin portion of HRT or a gross imbalance of the prescribed HRT …

Given the reasons women take or don't take HRT, it makes sense that women are interested in using HRT that is:

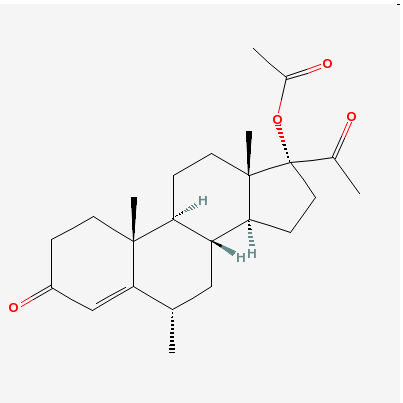
- Associated with fewer risks and side effects
- Perceived as "natural"
- Addresses long term health benefits
- Improves health and well-being

Bioidentical hormones are supplemental hormones that are exactly identical our biology. The chemical molecular structure is identical to hormones found in the human body. They are also referred to as "bio-equivalent", "human-equivalent", or "natural".

BHRT was used over 60 years ago and is the most prominent method of HRT in Europe. The hormone supplement is usually derived from soy or yam and made by a compounding pharmacy. The concept is to mimic nature by using substances naturally found in biologic systems, in physiologic doses.



Progesterone



Medroxy-Progesterone Acetate (MPA)
"Provera"

Diagram 8
Example of bioidentical vs. non-bioidentical chemistry

A note about nomenclature… A "progestogen" is a substance with progesterone activity. A "progestin" is a drug with progesterone activity. Progesterone is correctly called progesterone, whereas Provera and other non-bioidentical drugs are correctly called progestins. The media and many doctors skip over this little detail which is very specifically incorrect! We will see why this is so important as we analyze the risks and benefits of progesterone and progestins.

Maintaining hormone levels will provide relief of symptoms associated with hormone deficiencies and prevent many of the physical and mental changes associated with aging. Sounds good, but what are the risks? And, do bioidentical hormones provide the benefits without the risks?

It is contraindicated to take BHRT if one has an *active* or untreated breast, uterine or other hormone sensitive cancer. It is also contraindicated if there is no hormone deficiency.

Women's Health Initiative (WHI)

Many physicians such as me were studying and prescribing BHRT back in the early 1990s and earlier. Public awareness of HRT in general and interest in BHRT really started in 2002 with the bad news from the **Women's Health Initiative (WHI)** when National Institute of Health (NIH) prematurely halted the study after if was determined that that estrogen in combination with progestin increased a woman's risk of breast cancer, coronary events, stroke, and blood clots. Because so much of the current confusion and misinformation regarding HRT is based on this one study, it is worth taking the time to understand the results.

The WHI was a US government sponsored study designed to study risks & benefits associated with long-term hormone use (substitution). In this study, 16,608 healthy postmenopausal women with a uterus, ages 50-79, were randomized to either test or placebo group.

The HRT used in the WHI was not bioidentical. The test groups received estrogen alone (Premarin) or in combination with a progestin (PremPro). Premarin, which is derived from **pre**gnant **mar**es u**rin**e, is comprised of a mixture of sodium estrone sulfate and sodium equilin sulfate. The progestin component, Provera, is medroxy-progesterone acetate or MPA. Both drugs were given orally.

WHI Results in combination test group:

- 26% increased risk of invasive breast cancer
- 13% increased risk of non-invasive breast cancer
- 29% increased risk of heart attack or death from coronary disease
- 41% increased risk of stroke
- 200% increased risk of blood clot
- 33% reduced risk of hip fracture
- 37% reduced risk of colon cancer
- Relief of menopausal symptoms like hot flashes and vaginal atrophy

WHI Results in estrogen only test group:

- Increased risk of stroke and blood clots
- No change in risk of heart attack, colon cancer or breast cancer
- Reduced risk of hip fracture
- Relief of menopausal symptoms like hot flashes and vaginal atrophy

Note that 97.5% of women on treatment had *no* adverse events and the benefits from reduced hip fractures and colon cancer far offset the risk of breast cancers.

- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-333.

A follow up study from this data group, called the Women's Health Initiative Memory Study (WHIMS), showed a doubling in risk of developing dementia in women age 65 and older.

- Shumaker SA, et al. Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: The Women's Health Initiative Memory Study: a randomized controlled trial. JAMA 2003;289:2651-2662.

The WHI was a very good study in that it was a large randomized controlled trial (RCT) with good statistical methods. There were however many problems with WHI and WHIMS:

- Non-bioidentical hormones
- Wrong ratio of hormones
- Route of administration (oral)
- Age of participants (average age 63)
- Pre-existing disease in participants
- Irresponsible reporting by the NIH
- Inflating the risk of breast cancer by combining the RR statistics on invasive and non-invasive breast cancer to report the 40% increase risk in breast cancer
- Failed to insist on media coverage of the positive findings in the estrogen only arm of study
- Did not look at quality of life

As we continue in our analysis of studies on BHRT the problems with the WHI will become more apparent.

HRT & Breast Cancer

The first thing on most women's mind in regard to HRT safety is the risk of breast cancer. Does estrogen *alone* cause breast cancer?

A review of ten of the largest studies on this issue shows that the relative risk of developing breast cancer when taking estrogen alone, in various forms, ranges from 0.5 to 1.5 times the risk when not taking estrogen. The relative risk from these studies averages around 1 – which means that there does not appear to be a risk of breast cancer from estrogen alone. Clearly is it hard to justify saying estrogen HRT alone causes breast cancer.

- **WHI** – RR 0.77
- **BCDDP** – RR 1.36
- **Nurses Health Study** – RR 1.0, RR 1.46 in alcohol users
- **LA Cancer Surveillance** – RR 1.14
- **NHANES** – RR 0.5 (4 yrs), RR 0.8 (>10 yrs)
- **Iowa Women's Health Study** – RR 1.13
- **4 States** – RR 0.7
- **Collaborative Group** – RR 1.3 (5-9 yrs), RR 1.24 (>10 yrs)
- **Washington State** – RR 1.0 (12-15 yrs), RR 0.5 (>15 yrs)

However, there is more to the story, much more… We know estrogens stimulate breast growth, and there are several things we do know about estrogens and cancer. Consider the two estrogen receptors, different types of estrogens, estrogen dominance, and estrogen metabolites. Also, consider that progesterone protects the breast, whereas medroxy-progesterone (MPA) or Provera does indeed promote breast cancer, as highlighted in the WHI. Last we must address the negative impact of copious amounts of xenoestrogens, or false estrogens, in the environment and the positive role of some estrogenic compounds such as soy.

Estrogen Receptors

One of the most important elements in breast cancer prevention, and in applying safe methods for hormone replacement therapy (HRT), is in understanding the role of **estrogen receptors** in the body.

There are two estrogen receptors subtypes, estrogen receptor alpha (ERα) and estrogen receptor beta (ERβ), and they found in most every organ system in the body of both men and women. Cancers are always involved with ERα. Estrogens and similar chemicals will bind to ERα and stimulate breast tissue proliferation and growth, whereas ERβ will inhibit proliferation and prevent breast cancer.

There are three types of estrogens; estrone (E1), estradiol (E2) and estriol (E3). E2 will equally bind and activate ERα and ERβ, while E1 strongly binds to ERα at a 5:1 ratio, thus causing significantly increased proliferation of breast tissue. E3 will bind to ERβ at a 3:1 ratio thus having potential for breast cancer prevention.

Prior to menopause, women have equal ERα and ERβ expression, whereas after menopause the ratio changes showing increased ERα sites. Furthermore, E3 is the most prevalent estrogen prior to menopause, but is replaced by E1 as the dominant estrogen

after menopause. Thus, one can appreciate that the conditions for breast cancer increase after menopause due to increased ERα expression and the increased ratio of E1.

Friendly Estriol

Remember that E3 comprises about 80% of a woman's total estrogen up until menopause, when it shifts to become only 10-20% of circulating estrogen. Estriol is a weak, friendly estrogen that protects against cancer. There have been numerous studies over the last 30 years or more showing the safety of E3, which also has benefits for the heart, bone, and vaginal area and urinary system.

High levels of E3 during pregnancy correlate with less breast cancer, and other studies show that in general, higher levels of E3 correlate with less breast cancer. E3 has been shown to be the only form of estrogen *not* associated with increased risk of breast cancer.

E3 is an estrogen and an anti-estrogen.* It does this by binding *weakly* and only for a short time to ERα receptors, thus E3 does not effectively stimulate cellular transcription and proliferation of breast tissue – however, by occupying the receptor site it effectively blocks E1 and E2 from binding and stimulating the receptor. In this way, it is a weak estrogen *and* an anti-estrogen.

Research summaries show:

- Women with breast cancer have low E3
- Reduced Estriol excretion in patients with breast cancer prior to endocrine therapy. Lemon HM, JAMA, 1966, 196;1128-1136.

- E3 stopped metastatic breast cancer in 37% of women treated
- Lemon HM, Cancer Res 25, 1975; 1341-1353

- E3 alone reduces the rate of breast cancer
- Lauritzen, Acta Endocrinologica 38, 1961; 73-87

- Vit E increases E3 18% and lowers breast cancer risk
- Endocrine parameter and alpha-tocopherol therapy in patients with mammary dysplasia. London RS, 1981 Cancer Res 41; 3811-3813

- E3 inhibits receptors in breast tissue that stimulate cancer
- Mol Cell Endocrinol. 2010 May 14;320(1-2):162-70. Epub 2010 Feb 6. Estriol acts as a GPR30 antagonist in estrogen receptor-negative breast cancer cells. Lappano R et al

Thus, I recommend the use of E3 when replacing women's hormones. The safe and effective use of E3 for treating the symptoms of menopause has been established in many studies. There are no accounts of increased breast cancer associated with the use of E3 and in fact there are studies that show it reduces the development of breast cancer equal to that of one of the leading oncology drugs, tamoxifen, but without the side effects of tamoxifen.

There is little need to measure serum levels of E3 prior to taking HRT as the E2 level is proportionate to E3. However, E3 and E2 levels should be measured when taking HRT to insure a physiologic ratio is achieved.

When prescribing HRT the inclusion of E3 is a critical part of creating a safe and effective hormone balance. At the behest of the pharmaceutical industry the FDA has tried to remove E3 from the marketplace. This type of back-door politics between government and big business is creating a less-safe situation for women trying to safely replace their hormones, and is considered criminal by many experts in the field of HRT.

Estrogen Dominance

When estrogen is dominant, when it is not balanced by its sister progesterone, then it is "allowed" to over-stimulate the breast and increase the risk of cancer. This issue may more reflect the protective nature of progesterone.

Women who have a defective corpus luteal phase of the menstrual cycle never make normal amount of progesterone. Low levels of progesterone have been associated with increased risks of breast cancer. A 33 year study of 722 women diagnosed with infertility and luteal phase defect with progesterone deficiency showed a 10x risk of death from all cancers and 5.4x risk premenopausal breast cancer.

- Cowan LD, Gordis L, Tonascia JA, Jones GS. Breast cancer incidence in women with a history of progesterone deficiency. *Am J Epidemiol* 1981;114:209-217.

Poor Estrogen Metabolism

Estrogens are eventually broken down and metabolized by the liver prior to elimination. These normal metabolites can be altered in such a way that promotes breast cancer.

Under normal circumstances 99% of estrogens are methylated prior to safe excretion. This is done through the catechole-methy-transferase (COMT) pathway, and requires adequate methyl donors such as SAMe and methylcobalamin (B12). About 1% of estrogens are processed through the peroxidase pathway to form estrogen-quinones (EQ). These EQs have been shown to cause breast cancer if the wrong ones are produced.

Unfavorable estrogen metabolites include 4-hydroxy-estradiol (4OH-E2) and 16-hydroxy-estrone (16OH-E1). Favorable estrogen metabolites include the 2-hydroxy-estradiol (2OH-E2) and the methylated 4-methoxy-estradiol and 2-methoxy-estradiol.

Women metabolize estrogen poorly for several reasons including genetics, exposure to pesticides and toxins, excess estrogen, low thyroid, and impaired methylation capacity in

the liver. Poor gut health and lack of beneficial bacteria in the gut can impact estrogen metabolism as well.

Research summary shows:

- High levels of 4OH-E2 and 16OH-E1 relative to 2OH-E2 are associated with increased risk of breast ca.
- Breast cancer tissue has much higher amounts of 4OH-E1 than 2OH-E2 or 16OH-E1 concentrations
- 4OH-E1 forms Quinones which covalently bind DNA to cause depurination (shown to activate *ras* oncogenes)
- 4OH Equilenin (horse analog of 4OH-E1) is a more potent transforming agent than 4OH-E1 in vitro

The COMT pathway in the liver also methylates our stress hormone adrenalin. When exposed to prolonged stress this leaves the COMT pathway less available to manage estrogen metabolism in the healthiest manner, by methylation. This is one way that prolonged stress may lead to more cancers. Lowering stress effects may be one way to improve cancer risk.

The point in this little chemistry diversion is that estrogen metabolites can be easily measured using either serum or urine testing and improved through basic supplementation.

- Indole-3-Carbinol (I3C) and DIM, found in cruciferous vegetables, will favor 2OH-E2 pathway

Supplements that can help make more cancer fighting 2OH-E2 include: methylcobalamin (B12), methylfolate (activate folate) and S-adenosylmethionine (SAMe). Indole-3-Carbinol (I3C) and DIM will also encourage healthy 2OH-E2 production.

Progesterone - the Breast Cancer Shield

Progesterone naturally balances the stimulatory effect of estrogen in almost every way, and this is very evident with the issue of cancer. Women that do not make a normal amount of progesterone are at increased risk of uterine and breast cancer. Oddly enough, most doctors prescribing HRT will always put women on progesterone to protect the uterus from unopposed estrogen over-stimulation and increased cancer risk. Yet after a hysterectomy, many of the same doctors neglect to use progesterone, and instead prescribe only estrogen. This is a mistake that neglects to recognize the many roles of progesterone in balancing estrogen beyond the uterus, especially in regards to breast cancer protection.

There are numerous studies that show the protective role progesterone plays in breast cancer prevention, whereas synthetic progestins such as Provera (medroxy-progesterone acetate or MPA) *do* increase the risk of cancer.

Progesterone is shown to inhibit breast cell growth, increases survival in breast cancer patients, decrease cancer cell adhesions and cancer spread, and to suppress the metalloproteinase enzymes made by cancer cells which allow cancer to spread. MPA has the opposite effects.

- British J Cancer 1996; 73:1552-1555 / Chang KJ, Fertil Steril 1995; 63:780-791
- Cancer Res 2002;62:881-886 / WHI / BCDDP

There are numerous reviews that suggest progesterone and *some* progestins have a protective effect on breast tissue.

- Mauvais-Jarvis P, Kuttenn F, Gompel A, Benotmane A. Antiestrogen action of progesterone in the breast. *Pathol Biol (Paris)* 1987;35:1081- 1086. [Article in French]
- Mauvais-Jarvis P, Kuttenn F, Gompel A. Estradiol/progesterone interaction in normal and pathologic breast cells. *Ann N Y Acad Sci* 1986;464:152-167.
- Gorins A, Denis C. Effects of progesterone and progestational hormones on the mammary gland.
- *Arch Anat Cytol Pathol* 1995;43:28-35. [Article in French]
- Inoh A, Kamiya K, Fujii Y, Yokoro K. Protective effects of progesterone and tamoxifen in estrogen-induced mammary carcinogenesis in ovariectomized W/Fu rats. *Jpn J Cancer Res*
- 1985;76:699-704.
- Wren BG, Eden JA. Do progestogens reduce the risk of breast cancer? A review of the evidence.
- *Menopause J North Am Menopause Soc* 1996;3:4-12.

Low levels of progesterone have been associated with increased risks of breast cancer. A 33 year study of 722 women diagnosed with infertility and luteal phase defect with progesterone deficiency had 10x the risk of death from all cancers and 5.4x the risk of premenopausal breast cancer.

- Cowan LD, Gordis L, Tonascia JA, Jones GS. Breast cancer incidence in women with a history of progesterone deficiency. *Am J Epidemiol* 1981;114:209-217.

Progesterone, and NOT progestins such as MPA, provides a control mechanism to regulate the proliferative effects of estrogen. This means it prevents cancer.

- Chang KJ, Lee TT, Linares-Cruz G, et al. Influences of percutaneous administration of estradiol and progesterone on human breast epithelial cell cycle in vivo. *Fertil Steril* 1995;63:785-791.
- Formby B, Wiley TS. Progesterone inhibits growth and induces apoptosis in breast cancer cells: inverse effects on Bcl-2 and p53. *Ann Clin Lab Sci* 1998;28:360-369.
- Desreux J, Kebers F, Noel A, et al. Progesterone receptor activation – an alternative to SERMs in breast cancer. *Eur J Cancer* 2000;36:S90-S91.
- Malet C, Spritzer P, Guillaumin D, Kuttenn F. Progesterone effect on cell growth, ultrastructural aspect and estradiol receptors of normal human breast epithelial (HBE) cells in culture. *J Steroid Biochem Mol Biol* 2000;73:171-181.

A French study showed no increased risk of breast cancer in women using progesterone cream topically, and actually there was a reduced risk when adding a progesterone capsule.

- Plu-Bureau G, Le MG, Thalabard JC, et al. Percutaneous progesterone use and risk of breast cancer: results from a French cohort study of premenopausal women with benign breast disease. *Cancer Detect Prev* 1999;23:290-296.

Another French study showed no increased breast cancer risk when taking progesterone as opposed to synthetic progestins.

- de Lignieres B, de Vathaire F, Fournier S, et al. Combined hormone replacement therapy and risk of breast cancer in a French cohort study of 3175 women. *Climacteric* 2002;5:332-340.

Last, the largest study to date that most conclusively addresses the debate over progesterone and breast cancer. The French E3N-EPIC (European prospective investigation into cancer and nutrition) is a cohort study looking at over 50,000 women. It showed the same results as the WHI in women using synthetic progestins, a 1.26X relative risk (26% increase) for invasive breast cancer. But, it showed a 0.9X relative risk (a decrease!) in women using progesterone.

- Fournier A, Berrino F, Riboli E, et al. Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort. *Int J Cancer* 2005;114:448-454.

The bottom line is to adequately balance estrogen only with bioidentical progesterone, not with synthetic progestin "look-alike" drugs.

Xenoestrogens

We are exposed to many different estrogens, not only what we make in our bodies, but also those which are made in nature and industry. The types of estrogens not made in our bodies include phytoestrogens, mycoestrogens and xenoestrogens.

The plant form of estrogen is known as phytoestrogen. Often referred to as "dietary estrogens," phytoestrogens are present in such foods as linseed (flax), soy products, legumes and yams. Many over-the-counter menopause remedies such as soy and red clover contain phytoestrogens, also known as isoflavones. These are generally accepted as safe for women, and we have patients who find them helpful, but the data supporting their benefit for menopausal symptoms such as hot flashes is limited.

However, it is felt that the "weak" estrogens found in phytoestrogens play a protective role in our bodies, and a 2009 study in the Journal of the American Medical Association confirms that "among women with breast cancer, soy food consumption was significantly associated with decreased risk of death and recurrence." Another 2009 study which included over 70,000 women, from the American Journal of Clinical Nutrition, showed that "women who consumed a high amount of soy foods consistently during adolescence and adulthood had a substantially reduced risk of breast cancer."

Mycoestrogens are also a natural form of estrogen, made from fungi (i.e. mushrooms). Mycoestrogens do not appear to have effects on humans but a toxin they produce called

"mycotoxin" has been harmful to certain types of livestock and may produce allergy reactions in humans.

Xenoestrogens or "false estrogens" are industrially made compounds. They differ in their chemical structure from naturally occurring estrogens but they can act like estrogen in the body of both women and men. Unlike the phytoestrogens, evidence suggests that xenoestrogens are harmful to human health.

Xenoestrogens have been introduced into the environment by many industrial, agricultural and chemical companies, and are found in foods, drugs, cosmetics, insecticides, herbicides, plastics, oils, paints and adhesives. Although the environmental effects of xenoestrogens are a concern, your greatest exposure may be from common products in foods, food containers and personal care products. Just a few examples include:

- Butylated hydroxyanisole, BHA (food preservative)
- Erythrosine (food coloring FD&C Red No. 3)
- Bisphenol A, BPA (polycarbonate plastic denoted as #7, #3 or PC on the recycling symbol)
- Polychlorinated biphenyls, PCBs (electrical oils, lubricants, adhesives, paints)
- Ethinylestradiol (birth control products)
- 4- Methylbenyzlidene camphor, 4-MBC (sunscreen lotions)
- Parabens, commonly known as methylparaben, ethylparaben, propylparaben and butylparaben (cosmetics, lotions and shampoos)

We have seen some amazing cases of hormonal imbalance in which reducing exposure to xenoestrogens has proven to be the remedy. For example, if you are a woman with signs of "estrogen dominant" menstrual cycles, which includes symptoms such as PMS, water retention, tender breasts, or heavy painful menses, then you should try eliminating your exposure to xenoestrogens. If that does not help then you might have a hormone imbalance such as low thyroid or low progesterone.

Avoiding xenoestrogens can be achieved through reading labels and being aware of what you are buying. Many cosmetics are now labeled "paraben free." You may notice plastic containers stating they are "BPA free." You can also look for food and beverage containers that have the recycling number "1" or "2" in addition to looking for glass and stainless steel alternatives to plastic. It may also be a good idea to go through your pantry and kitchen drawers looking for unwanted plastic containers. As a rule, never heat Styrofoam or any plastics in the microwave.

It is good practice to read all food labels. When I see ingredient lists that look like "paragraphs" then that food does not go into my basket. Avoid processed and pre-packaged foods when you can. If you look for fresh, preferably organic fruits,

vegetables, and natural meats, you will not only be avoiding xenoestrogens but will also have the bonus of choosing a healthier diet.

There is a general consensus in the literature that xenoestrogens artificially stimulate estrogen receptors, causing early puberty in young girls, feminization in young boys, increasing breast cancer rate in women and prostate cancer rate in men.

"…xenoestrogens may play a significant role in the development of breast cancer."

- Med Hypotheses. 1998 Jun;50(6):457-64. Xenoestrogens significantly enhance risk for breast cancer during growth and adolescence. Ardies CM, Dees C

"…xenoestrogens have been shown to cause breast cancer and also induce the expression of hormone receptors in vitro and in vivo. … xenoestrogens could be the important cause of high and increasing rates of hormone receptor positive breast cancer across the world. New research in the area of mammary stem cells provides added indication of the probable time period of exposure to xenoestrogens with chronic exposure later in life leading to hormone receptor positive breast cancer and most probable reason behind increasing breast cancer incidence."

- Med Hypotheses. 2009 Jun;72(6):652-6. Epub 2009 Jan 19. Xenoestrogens may be the cause of high and increasing rates of hormone receptor positive breast cancer in the world. Dey S, Soliman AS, Merajver SD.

It is suggested that living in an urban area exposes women to more xenoestrogens, causing a significant increase in estrogen receptor (ER) positive breast cancers.

"Urban ER+ incidence rate (per 100,000 women) was 2-4 times higher than rural incidence rate. ER-incidence rate was 2-3 times higher in urban areas than in rural areas. Our findings indicate that urban women may probably have a higher exposure to xenoestrogens."

- Breast Cancer Res Treat. 2010 Feb;120(1):149-60. Epub 2009 Jun 23. Urban-rural differences in breast cancer incidence by hormone receptor status across 6 years in Egypt. Dey S, et al.

"Human epidemiological studies and experimental animal data strongly suggest that xenobiotics with estrogenic activity may participate in to the increasing incidence of breast cancer."

- Gynecol Obstet Fertil. 2008 Oct;36(10):969-77. Epub 2008 Sep 19. Environmental endocrine disruptors and breast cancer: new risk factors? Fénichel P, Brucker-Davis F.

Soy

Soy can also play a huge role in the prevention of breast cancer, but it is a misunderstood food source that needs clarification. Soy is a phytoestrogen, which is a plant-derived chemical that is similar to estrogen. Soy phytoestrogens are NOT estrogens nor do they act like estrogens. Soy phytoestrogens are more like anti-estrogens that bind to ERβ with a 20:1 affinity over ERα and in addition they will increase the number of ERβ and decrease the ERα in cells. More ERβ sites equal less cancer!

When talking about the benefits of soy, I am referring only to FERMENTED forms of soy, which include:

- **Tempeh** a fermented soybean cake with a firm texture and nutty, mushroom-like flavor
- **Miso**, a fermented soybean paste with a salty, buttery texture
- **Natto**, fermented soybeans with a sticky texture and strong, cheese-like flavor
- **Soy sauce**, which is traditionally made by fermenting soybeans, salt and enzymes

Fermented soy will improve estrogen metabolism by decreasing the amount of cancer promoting metabolites. It will also increase the P53 tumor suppressor gene expression, increase the BRCA1 and BRCA2 gene expressions and decrease the HER2 gene expressions. Women with low BRCA1 and BRCA2 gene activity have a higher rate of breast cancer, and decreasing the HER2 gene expression will slow breast cancer growth.

Older men are prone to prostate cancer, have higher estrogen levels than women of the same age, and increased ERα sites on prostate cells. This leads to more cancer. Again, soy will increase the ERβ sites on tumor cells in breast, prostate, and even ovarian cancers.

Unfermented soy products, including tofu, and processed soy products like soymilk, soy cheese, soy burgers and soy ice cream, are NOT healthy. There are thousands of studies showing unfermented soy is linked to digestive disturbances, immune dysfunction, thyroid disorders, hormone disruption and more! The billion dollar soy industry has a million dollar disguise in the advertising designed promote the health benefits of soy.

Learn about fermented soy. Tempeh is like a "meat substitute", similar to the more commonly known tofu, typically cut into cubes and sautéed, baked or fried. Miso is usually found in miso soups, often paired with rice, and is also used in marinades and sauces. Natto is usually paired with rice and veggies, and flavored with everything from soy sauce to sugar. Natto has the benefits of soy, mentioned above, plus it has a positive blood thinning effect, and is high in Vitamin K which helps build strong bones.

Cooking with fermented soy is not hard, but it is not well known in our culture. The next time you shop, try something different and improve you health - add some fermented soy products to your list!

Summary on HRT and Breast Cancer

Estrogen replacement alone does *not* clearly increase the risk of breast cancer and the addition of bioidentical progesterone reduces the risk of breast cancer. Synthetic "look-alike" progestins such as Provera increase the risk of breast cancer. Estriol is cancer protective while estrones are cancer promoting. Estrogen metabolites can be cancer promoting and these can be measured and addressed. Exposures to cancer promoting xenoestrogens should be minimized and there are foods and supplements that can lower breast cancer risk.

HRT & Heart Disease

Women start making artery plaque after menopause in part due to the decline in ovarian hormones. Replacing estrogen early and staying on it long term will help prevent artery plaque formation and lower the risk of heart disease by as much as 50%.

Estrogen prevents plaque formation but can rupture existing plaque, thus it is critical to start estrogen replacement early after menopause before plaque has had time to develop. If estrogen is started after plaque has had time to form then it may cause plaque rupture and heart attack.

- Postmenopausal hormone therapy: new questions and the case for new clinical trials. Menopause. 2006 Jan-Feb;13(1):139-147
- Endogenous estrogen exposure and cv mortality in postmenopausal women. Am J Epidemiol 2002 Feb 15; 155(4):339-345

If a women wants to start HRT and it has been more than just a few years after menopause then it is imperative to screen her arteries for plaque and take measures to stabilize that plaque prior to starting HRT (see section on Heart Disease).

The earlier women start HRT the better when it comes to heart disease prevention. Several studies show the increased rate of heart disease in the first year after starting HRT followed by a decline in risk over time. This occurs in older women (age 65-67) and highlights the HRT causing plaque rupture in women that have existing unstable artery plaque. Note that the risk of heart disease is reduced 50% in the groups of younger women (age 50-59) who started HRT sooner.

- Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group.
- Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II).
- Nurses Health Study

The longer women stay on estrogen the better. Estrogen dilates blood vessels*, decreases the sympathetic nerve effect of tightening blood vessels* and decreases the thickening and inflammation that occurs with blood vessel disease*.

- A novel, nongenomic action of estogen on the cv system. J Clin Endocrinology Metab. 1998 Jul;83(7):2313-6
- Transdermal estrogen replacement therapy decreases sympathetic activity in postmenopausal women. Circulation. 2001 Jun 19;103(24):2903-8
- Clinically used estrogens differentially inhibit human aortic smooth muscle cell growth and mitogen-activated protein kinase activity. Arterioscler Throm Vasc Biol. 2000 Apr;20(4):964-72

The risk of blood clots depends on the type of estrogen and whether it is taken orally in a pill that one swallows or by another method, such as in a topical cream or sublingual tablet. Estriol reduces the risk of blood clots and *not* taking estrogens in an oral pill reduces the risk of clotting.

- Transdermal estrogen replacement therapy: beneficial effects of hemostatic risk factors for cv disease. Maturitas. 1996 May;24 (1-2):43-50
- Comparison of transdermal and oral estrogen-progestin replacement therapy: effects on CV risk factors. Menopause. 2001 Sep-Oct;8(5):347-52
- Effects of oral and transdermal estrogen/progesterone regimes on blood coagulation and fibrinolysis in postmenopausal women Arterioscler Thromb Vasc Biol. 1997 Nov;17(11):3071-8

- Estriol in the management of the menopause. JAMA. 1978 21;239(16):163-41

A Mayo clinic study shows estrogen replacement correlates with less artery plaque, as measured by cardiac CT scanning of coronary artery plaque.

- Estrogen status correlates with the calcium content of coronary atherosclerotic plaques in women. J Clin Endocrinology Metab. 2002 Mar;87(3):1062-7

The synthetic progestin clearly worsens heart disease as studies show adding provera to estrogen replacement increases heart disease risk*. Bioidentical progesterone does not share these same side effects and in fact is shown to be beneficial for the heart and blood vessel system.

Heart healthy benefits of bioidentical progesterone show it:

- dilates blood vessels and prevents vessel spasm
- increases nitric oxide along with E2 which increases blood flow
- has no effect the inflammatory marker CRP
- lowers “bad” LDL cholesterol
- raises “good” HDL cholesterol
- inhibits the smooth muscle around vessels from thickening
- inhibits receptors that attract inflammatory cells into artery plaque

- The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. The Writing Group for the PEPI Trial.
- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women’s Health Initiative randomized controlled trial. *JAMA* 2002;288:321-333.
- Rosano G, et al, J Am Coll Cardiology 2000; 36:2154-9
- Wakatsuki A, Circulation 2001; 102:1773-8
- Miyagawa K et al, Nat Med 1997; 3:324-7
- Molinari C, et al, J Vasc Res 2001; 38:569-77
- William JK et al, J Am Coll Cardiology 1994; 224:1757-61
- Cushman M, et al, Circulation 1999; 100:717-22
- Seeger, Menopause 2001;8:5-9
- Carmody B, et al, J Vasc Surg 2002;36:833-8

Summary on HRT and heart disease

Early use of any estrogen reduces risk of heart disease and stroke, bioidentical progesterone is protective while synthetic MPA increases risk, and topically administered hormones have less effect on clotting factors in the liver.

HRT & Bone Health

Estrogen and progesterone are necessary for strong bones. This is the least controversial area regarding hormone replacement.

During our life, our bones are constantly being remodeled, with bone building cells called osteoblasts and bone cells that break-down bone, called osteoclasts. The balance of these

two cell lines determines whether we build bone or ultimately break-down bone, whether our bones get stronger or weaker.

The thinning of bone with aging is primarily due to hormone decline. When our bone density is 1.5 standard deviations below normal, it is called *osteopenia*, or thinning of bone. When the bone density falls 2.5 standard deviations below normal, then it is called *osteoporosis*, or brittle bone.

Osteoporosis is a much bigger problem than most people recognize. 1 in 3 women over age 50 will experience an osteoporotic fracture in their lifetime.

- Melton LJ, 3rd, Chrischilles EA, Cooper C, et al. (1992) Perspective. How many women have osteoporosis? J Bone Miner Res 7:1005.

The lifetime risk of osteoporosis and fracture is 40%, equal to the risk of the leading cause of death, cardiovascular disease.

- Kanis JA (2002) Diagnosis of osteoporosis and assessment of fracture risk. Lancet 359:1929.

In white women, the lifetime risk of hip fracture is 1 in 6, compared with a 1 in 9 risk of a diagnosis of breast cancer.

- Cummings SR and Melton LJ (2002) Epidemiology and outcomes of osteoporotic fractures. Lancet 359:1761.

Estrogen is well known to slow bone loss by increasing the activity of the bone building cells, the osteoblasts. Recent research suggests that estrogen helps keeps osteoblasts alive by binding to ERbeta and turning off the genetic switch that activates an enzyme which promotes the programmed death of osteoblasts.

- Physiol Behav. 2010 Feb 9;99(2):181-5. Epub 2009 May 5. Estrogen regulation of apoptosis in osteoblasts. Bradford PG, Gerace KV, Roland RL, Chrzan BG

The same researchers found that phytoestrogens from soy (genistein and daidzein) also promoted ERbeta activation as did E2, without activation of ERalpha. The results provide a basis for understanding how dietary phytoestrogens protect bone without increasing the risks for breast cancer.

- Mol Nutr Food Res. 2007 Feb;51(2):171-7. Phytoestrogens activate estrogen receptor beta1 and estrogenic responses in human breast and bone cancer cell lines. Chrzan BG, Bradford PG.

Estrogens also slow the resorption or breaking-down of bone by the osteoclasts. Even the weak, friendly E3 has also been shown to protect bone. The exact mechanism for this beneficial effect on the activity of osteoclasts is under intense investigation. It is not clear whether estrogen improves bone density by direct or indirect effects on the bone cells.

- J Gerontol A Biol Sci Med Sci. 2000 Apr;55(4):B183-90; discussion B191-3. Estriol (E3) replacement improves endothelial function and bone mineral density in very elderly women. Hayashi T, Ito I, Kano H, Endo H, Iguchi A.
- Tzingounis VA, JAMA 1978 Apr21; 239:1638-41
- Ratz, NEJM 1993 Sep 9;329(11):802-3
- Mol Endocrinol. 2010 May;24(5):877-85. Epub 2009 Nov 12. Minireview: osteoprotective action of estrogens is mediated by osteoclastic estrogen receptor-alpha. Imai Y, Kondoh S, Kouzmenko A, Kato S.

Progesterone exerts a positive influence on the bone building osteoblasts and has been shown in many studies to increase bone density.

- Prior JC, Endocrin Rev 1990;11(2):386-398
- Prior JC, et al, Am J Med 1994;96:521-30
- Prior JC, et al, J Bone Miner Res 1997;12:1851-63

The osteoblasts have the ability to convert progesterone into anabolic steroids which have bone-building properties.

- Horm Metab Res. 2008 Oct;40(10):679-84. Epub 2008 Jun 6. Progesterone is extensively metabolized in osteoblasts: implications for progesterone action on bone. Quinkler M, Kaur K, Hewison M, Stewart PM, Cooper MS.

Women can experience loss of bone many years prior to menopause due to the natural decline in progesterone, while supplementing the missing progesterone will improve the bone loss.

- J Osteoporos. 2010 Oct 31;2010:845180. Progesterone and bone: actions promoting bone health in women. Seifert-Klauss V, Prior JC.
- J Clin Densitom. 2004 Spring;7(1):85-92. Bone densitometry in premenopausal women: synthesis and review. Khan AA, Syed Z.
- Pharmacotherapy. 2009 Mar;29(3):305-17. Osteoporosis risk in premenopausal women. Vondracek SF, Hansen LB, McDermott MT.

Summary on HRT and Bone

While the science unravels the exact mechanism for hormone benefits to bone, there is no question that estrogen and progesterone help maintain and rebuild strong bones. Estrogen slows bone loss while progesterone will add to bone density. Be especially alert to the premenopause condition of low progesterone and screen for bone loss earlier than usually anticipated. In these cases evaluate for other causes of bone loss (see Bone Health). Testosterone is another important bone-building hormone for men and women (see Testosterone).

HRT & Brain Health

Estrogen stimulates the brain, with increases in excitatory neurotransmitters, including serotonin, dopamine, epinephrine and norepinephrine, all of which contribute to energy, mood, and cognitive processing. Progesterone will naturally balance estrogen effects on the brain to prevent over-stimulation by signaling the calming GABA receptors.

Declining hormones will affect brain function and the hormones have a protective effect on brain neurons. If started early and continued HRT will increase cognitive function and protect against Alzheimer's dementia.

- JAMA. 2001 Mar 21;285(11):1489-99. Hormone replacement therapy and cognition: systematic review and meta-analysis. LeBlanc ES, Janowsky J, Chan BK, Nelson HD.
- JAMA. 2002 Nov 6;288(17):2123-9. Hormone replacement therapy and incidence of Alzheimer disease in older women: the Cache County Study. Zandi PP, et al.
- Cognitive and MRI effects of estrogen therapy. Menopause Vol 13, No 3, Oct 2006, 411-22
- JAMA. 2004 Jun 23;291(24):3005-7. Estrogen and dementia: insights from the Women's Health Initiative Memory Study. Schneider LS.

Aside from the long term protective effects on the brain, HRT will help maintain a positive mood, energy, and mental processing. Many women report depression, anxiety or "brain fog" after menopause, and this is relieved with HRT.

HRT & Other Areas

HRT has been shown to lower the rate of **colon cancer**. HRT slows the progression of **osteoarthritis**, protecting against cartilage loss and is important for cartilage health. HRT will prevent **vaginal atrophy** and the secondary issues of urinary incontinence and urinary infections. HRT also has beneficial effects on **body composition** helping to increase body muscle mass while lowering body weight and body fat content.

- Gynecol Endocrinol. 2007 Oct;23 Suppl 1:42-4. Long-term use of progestogens: colon adenoma and colon carcinoma. Schindler AE.
- BMC Cancer. 2007 May 8;7:76. Colon cancer risk and different HRT formulations: a case-control study. Dinger JC, Heinemann LA, Möhner S, Thai do M, Assmann A.
- Maturitas. 2010 Sep;67(1):29-33. Menopausal arthralgia: Fact or fiction. Magliano M.
- Womens Health (Lond Engl). 2005 Jul;1(1):125-32. The clinical potential of estrogen for the prevention of osteoarthritis: what is known and what needs to be done? Tankó LB, Karsdal MA, Christiansen C.
- Acta Histochem Cytochem. 2007 Feb 27;40(1):27-34. Epub 2007 Feb 5. Localization of estrogen receptors alpha and beta in the articular surface of the rat femur. Oshima Y, et al.
- Climacteric. 2010 Sep 30. Recommendations for the management of postmenopausal vaginal atrophy. Sturdee DW, Panay N.
- Cochrane Database Syst Rev. 2006 Oct 18;(4):CD001500. Local oestrogen for vaginal atrophy in postmenopausal women. Suckling J, Lethaby A, Kennedy R.
- J Appl Physiol. 2009 Jul;107(1):25-33. Epub 2009 Feb 26. Postmenopausal hormone replacement therapy modifies skeletal muscle composition and function: a study with monozygotic twin pairs. Ronkainen PH, et al.
- J Endocrinol Invest. 2003 Sep;26(9):893-901. Body composition and muscle performance during menopause and hormone replacement therapy. Sipilä S.
- Menopause. 1999 Winter;6(4):312-5. Impact of hormone replacement therapy on the body mass and fat compositions of menopausal women: a cross-sectional study. Sayegh RA, et al.

Step 5
Beginning Treatment
You're Most Exciting Step to Hormone Balance

Tips for knowing what hormone to take and how to take them

- Learn which methods of HRT are best
- Why not to take HRT in an oral pill
- Find out exactly what is in bioidentical and why it is formulated the way it is
- Learn what is a good starting dose of HRT
- Find out about a few secrets with progesterone
- Learn what a typical BHRT prescription should look like
- Tips on working with your doctor or finding one who will work with you

Treatment

Recent History of HRT

HRT is perhaps one of the most misunderstood and misguided areas in medicine. We use only bioidentical hormones for replacement with many common diseases, such as insulin with diabetes, cortisol with Addison's disease, thyroid with low thyroid, and growth hormone with growth hormone deficiency. How did we get so confused with HRT?

In the late 1930s the estrogen replacement called Premarin was developed by Ayerst laboratories in Canada, and in 1942 was approved by the FDA for use in the US. Premarin is derived from pregnant horses, getting its namesake from **pre**gnant **ma**res u**rin**e. For 60 years this was the predominant form of estrogen replacement, until the WHI blew the whistle on the negative effects of non-bioidentical HRT, especially condemning the progestin drug Provera.

These two non-bioidentical drugs were the mainstay of HRT for so many years, not because of their safety and efficacy, but because of the patent, the FDA approval, and a marketing campaign that evolved right along with the feminist movement, women's rights and women's health. The sad truth is that billions of dollars in profit is the reason these hormone "look-alikes" remained at the top of the list for HRT. That has changed and women are now in a much more powerful and well-educated position in regards to HRT, and in the true best interest of their health they are demanding a better option for HRT.

Getting Started

The first step in determining treatment is to analyze where a women is in the process of hormone decline. More important than laboratory testing for hormone levels is to understand the various patterns of hormone decline. I have seen many women mistreated due to the practitioner simply treating a number on a laboratory test, instead of treating the patient based on the obvious stage of hormone decline. Furthermore, people have different sensitivities to hormones, such that for a given blood level, one patient has symptoms of too much hormone while another has symptoms of too little hormone. In this case adjust the hormone to the patient and not to the lab test. Let's take a look at the common hormone patterns.

Pre-Menopause Estrogen Dominance

If a woman is still having menstrual cycles, then there is usually enough estrogen present, and there are often signs of progesterone decline. In this case taking progesterone 2-3 weeks, then stopping for a week during menses, is usually indicated. This is called "progesterone cycling".

Progesterone is commonly the first hormone to be replaced since it is often the first to decline. It is given to balance the remaining estrogen. Women in this situation often present with increasing signs of estrogen dominance. Ovulation might not occur every month thus some women will skip cycles, or have irregular cycles both in frequency and in degree of bleeding.

Prescribing progesterone cycling will usually completely eliminate the signs of estrogen dominance, both lowering the physical risks associating with estrogen dominance, and relieving the disturbing symptoms of estrogen dominance.

Refer back to diagram 7 outlining the hormone levels during a typical 28 day menstrual cycle, and it should make sense why we prescribe progesterone for several weeks to balance the natural rise of estrogen. The exact number of days progesterone is taken is a bit variable, but we try to use at least 2 weeks in the cycle.

It is helpful to consider three aspects of the estrogen dominant cycle when determining how to cycle progesterone – the menses, the physical symptoms of estrogen dominance, and the mental symptoms of estrogen dominance.

When treating only mood changes, I may utilize progesterone for only a few days or a week prior to menses, such as day 21-28. Some women feel anxious or irritable just prior to menses, and it is often relieved with targeting progesterone only on those days.

Along the same lines as mood disorders, the physical symptoms of estrogen dominance may present for only a few days or a week prior to menses, and again the progesterone may be given only on those days, right up to day 28.

But when treating the heavy estrogen dominant menstrual cycle, progesterone usually needs to be introduced earlier in the cycle, in order to counter the rise in estrogen right from the beginning. Again, referring to diagram 3 one notes that estrogen starts rising just after the menses and peaks about day 12 in a 28 day cycle. Thus, we will start progesterone around day 7-10 and continue to day 28, in cases of heavy menses. This will protect the uterus from estrogen over-stimulation. A similar logic is used with physical condition of breast cysts and fibroadenomas, both of which are found with excess estrogen.

Peri-Menopause

Right before, during, and after the last menstrual period is the peri-menopause. This is the time "around menopause" and is fraught with whacky erratic changing hormone levels. This is the beginning of estrogen withdrawal symptoms such as hot flashes, night sweats and mood swings. It is difficult to treat women in this stage because their own hormone production is changing from month to month, and like a sputtering engine, it may be up one month, low the next, then back up again the next, before finally quitting altogether.

During this time, we usually start with progesterone cycling, and within a few months can determine if it is time to bring in estrogen as well. If the progesterone cycling does not take care of the early estrogen withdrawal symptoms then estrogen is also introduced. If progesterone cycling does take care of the early signs of falling estrogen, then we will continue this until the withdrawal signs return or the menses stops, at which point estrogen is introduced.

Attempts at continuous therapy during this phase may be futile, as the body is still cycling enough to cause menses. In this case we will cycle estrogen and progesterone, with the patient being on them for 21 days then off for 7 days during menses.

A note here that bioidentical hormones, particularly progesterone, are not nearly as potent as the synthetic drugs, such as Provera, or birth-control pills. Some practitioners will use birth-control pills during this phase to "over-ride" the changing hormone cycles, until a few years pass and the pituitary-ovary system is in post-menopause. Given the risks of birth-control pills, and the wishes of women to avoid synthetic non-bioidentical hormones, I do not recommend this approach unless absolutely necessary.

Post-Menopause

After the last menstrual cycle, both estrogen and progesterone are low, and both need to be replaced. This is usually done by daily doses without a break and is called "continuous therapy". The level of estrogen and progesterone need to be balanced, so

that the body does not experience dominance of either hormone. The uterus should be in a dormant state and neither encouraged to proliferate (grow) under the influence of excessive estrogen, nor secrete (mature for pregnancy) under excess influence of progesterone.

Once the proper balance of estrogen and progesterone is achieved, there is usually a need to make minor adjustments the first few years after menopause, but in subsequent years the HRT will typically remain the same stable dose.

What about Testosterone?

Testosterone is a "wild card" in that it may drop out many years before menopause or many years after menopause. It will, however, most usually disappear along with estrogen right around menopause. Based on symptoms of low testosterone we usually recommend testing a serum level and replacing testosterone. It is recommended to wait on testosterone until progesterone cycling is well established for a few months or until continuous estrogen/progesterone is well balanced. Then, bring in testosterone slowly and increase the dose to desired affect.

There are two reasons to wait on testosterone until estrogen and progesterone are stabilized. One, it is simpler to manage one thing at a time, and should there be side effects it is easier to sort out without testosterone immediately in the mix. Two, testosterone is the immediate precursor to estradiol. This means that when adding testosterone into the mix, sometimes it will convert and significantly raise the estradiol levels. In this case the estradiol component is simply reduced while the testosterone is raised to its desired level.

For a premenopausal woman with estrogen dominance, starting to cycle progesterone in order to balance estrogen, it is best to get the estrogen dominance under control for a few months before bringing in testosterone. Otherwise one could risk having the testosterone convert to estrogen and increase the estrogen dominance before the progesterone was established.

For a postmenopausal woman starting continuous estrogen and progesterone, it is best to get the "sisters" balanced before bringing in testosterone. If there are symptoms of irritability or agitation, it is difficult to tell if it is from too much estrogen or testosterone. Occasionally women who are balanced and stable on estrogen/progesterone will start testosterone then start noting signs of estrogen dominance such as breast tenderness, water retention, or uterine bleeding. In this case it is easier to recognize that testosterone is converting to estrogen and quickly lower the estrogen while continuing to increase testosterone to desired level.

The whole issue of testosterone converting to estrogen is not common – it seems to occur only in about 1 in 50 women – but the above reasons are the logic behind waiting to introduce testosterone carefully after estrogen and progesterone are on board.

Why Not To Take HRT by the Oral Route

I recommend to *not* take ovarian hormones orally, in which a tablet or capsule is swallowed, and absorbed in the intestine. When this happens, the hormone is first sent to the liver for processing, which is called "1st pass metabolism" meaning it is metabolized in the liver prior to being sent on the rest of the body. Interestingly, with some hormones this is not an issue, such as with thyroid hormone replacement, but with the ovarian hormones there are numerous reasons to avoid 1st pass metabolism.

First of all, with estrogen, 1st pass metabolism leads to poor absorption, as a large portion is metabolized before ever getting through to the blood stream. I have seen numerous women on huge doses of oral estrogen still suffering from estrogen deficient symptoms due to a low serum level of estrogen.

Second, the liver detects a "tsunami" of estrogen and properly makes more binding proteins to bind the estrogen in the bloodstream. The problem now is this high level of binding protein will also bind up other hormones such as thyroid and testosterone, inducing an artificial lowering of those hormones. Many women placed on birth-control pills or oral estrogen HRT will gain weight due to the low thyroid state caused by giving hormones though the oral route. This is why some birth-control can be used to treat acne, as it will lower testosterone levels secondary to the high binding proteins.

The oral route is also hard on the liver since it has to process an unusual amount of hormones. This will cause an increase in blood clotting factors, particularly with Provera. The strain will lead to sludging of bile in the gallbladder and many women have last their gallbladder secondary to taking oral estrogens.

- JAMA. 2005 Jan 19;293(3):330-9. Effect of estrogen therapy on gallbladder disease. Cirillo DJ, et al.
- Harv Womens Health Watch. 2008 Oct;16(2):6-7. Hormone therapy: gallbladder risk is lower with a patch than a pill.
- Ann Intern Med. 2001 Oct 2;135(7):493-501. Effect of estrogen plus progestin on risk for biliary tract surgery in postmenopausal women with coronary artery disease. The Heart and Estrogen/progestin Replacement Study. Simon JA, et al.

The insulin sensitizing benefits of estrogen are not realized when taking estrogen orally. This will encourage insulin resistance and diabetes, and secondarily increased risk of artery disease.

Last, oral administration of estrogen encourages metabolism to estrone and quinolone metabolites which, as outline previously, increases cancer risk.

Progesterone does not seem to have the negative health risks when given orally, but it does have a special issue to consider. The 1st pass metabolism on progesterone causes

about 90% of the progesterone to be converted to very sedating metabolites. This is not a desirable side effect and makes it more difficult to achieve a good serum level of progesterone. In cases of insomnia, especially when awakening in the middle of the night, I will sometimes try oral progesterone to purposely increase the levels of sedating metabolites. While this is a reasonable, safe strategy, it is important to search for and treat other causes of insomnia.

Of note, bioidentical progesterone, even when given orally, does *not* cause an increased risk of blood clots, heart attack or stroke. This is contrary to Provera.

Delivery Methods

I recommend HRT be given by way of transdermal creams (topical) or sublingual tablets (under the tongue). Either route avoids the 1st pass metabolism and delivers the hormone directly into the blood stream. Other acceptable routes include subcutaneous pellet implants, vaginal or rectal suppositories, or injections.

The "sisters", estrogen and progesterone, are always started first and adjusted until the dose is stable. Then testosterone is slowly introduced (see Testosterone) later for two reasons. One, so that only one hormone is being added at a time, and if side effects such as irritability present, then the dose of testosterone is lowered, and two, testosterone will convert to estrogen. If a woman was previously doing well on estrogen and progesterone, then after adding testosterone she notes signs of estrogen dominance, such as breast tenderness or water retention, we know to lower the estrogen dose and keep increasing the testosterone to its desired level.

Initially, I recommend keeping all three hormones separate until the dose is stable, then we combine them into one cream or tablet. This allows for independent adjustments to any of the individual hormones. Most of my patients will take HRT twice daily to get a smooth blood level. The creams tend to enter into the bloodstream a little slower since the hormone pauses in the subcutaneous fat for 6-8 hours as it passes on into the bloodstream, whereas the sublingual tablets enter into the bloodstream very quickly. If a once daily dose is preferred, then the creams make more sense.

The second most common dosing method is to keep the progesterone separate and take it only at night time, either to help with sleep, or because it is not tolerated in the morning. Some women feel sleepy, groggy, dizzy or drunk shortly after taking progesterone. This is not common and most women love taking a morning dose of progesterone. As one patient said to me, she feels "calm but not fatigued" with her morning progesterone!

Sometimes we will formulate a morning dose of estrogen/testosterone and an evening dose of estrogen/testosterone/progesterone. Some women take estrogen/testosterone in

the morning and progesterone at night. Still others will take all three as a single dose in the morning or at night.

The bottom line is that I start with twice daily dosing in most women, unless sleep is a huge problem then I may leave the progesterone all for bedtime. Beyond that, women are quite astute at making dosing adjustments that feel right and best fit their bodies.

In cases of severe vaginal dryness we often start with a vaginal cream applied several nights / week. This gets the estrogen directly to the vaginal tissue and provides very quick relief of dryness and tenderness. After a few months of systemic HRT women are usually able to wean off the vaginal cream, although some will continue to use the vaginal cream indefinitely.

Dosing Guidelines

I start HRT doses based on an educated guess, taking into consideration a woman's size, body shape, medical history (particularly as relates to hormones), current symptoms and phase of hormone decline or imbalance.

Estrogen is responsible for breast development and for maturing bone development at puberty. Thus a short, buxom woman is more likely to make more estrogen and require higher dose HRT, while a tall woman with small breasts is likely to make less estrogen and thus require a smaller HRT dose. Fat cells will make estrogen, so a woman who is overweight may not need as much estrogen replacement. Estrogen dosing is somewhat proportionate to weight. A woman with a history of estrogen sensitivity, such as heavy estrogen dominant cycles, or premenstrual migraines, will often require a smaller dose of estrogen.

After starting HRT, my patients are educated to make minor adjustments based on their response. If they experience a side effect that is not obvious as to which hormone needs adjusted, then we check hormone levels. This is not common and is required in only about 1 in every 20-30 women. After a stable dose is achieved I like to obtain hormone levels to confirm that we are giving enough to maximize health benefits, and make any minor adjustments based on the lab results.

As noted earlier, the ultimate guide is the patient. Occasionally I will adjust the HRT dose based on a lab result and the patient does not do well with the change. In this instance, I treat the patient and not the lab test. This underscores that reference ranges on labs are based on a bell shaped curve of thousands of patients, and there is not a "one-size-fits-all" blood level for hormones.

HRT Ingredients and Doses

BHRT from compounding pharmacies is typically made from natural sources such as yam or soy. It has to be synthesized to make the powders that will be formulated into the final products. I recommend using "BiEst" which is a mixture of estriol and estradiol, as these are the main estrogens present in females up until menopause (see Estrogen Basics). BiEst is generally understood to be an 80:20 ratio of E3:E2 (based on early work of HRT pioneer Dr Johnathan Wright), but some practitioners use a 50:50 ratio (based on the later work of Dr Xu). The important thing is to ultimately check hormone levels of both estrogens and adjust the mixture accordingly to obtain a balanced ratio. Note that with BiEst as the total mg amount changes, the ratio of E3:E2 remains the same. E.g. BiEst (80:20) 1.25mg = E3 1mg + E2 0.25mg, and BiEst 5mg = E3 4mg + E2 1mg. A common total daily dose of BiEst is between 1.25mg and 5mg.

Progesterone is usually dosed proportionate to estrogen. That is, when using a small dose of estrogen one would use a small dose of progesterone. This underscores the concept of the "sisters" and finding a balance of the two hormones. Though, sometimes the dose of progesterone can be increased "above the balance" to overcome estrogen sensitivity. The opposite does not usually go well, that is increasing estrogen above the balance usually leads to estrogen dominant symptoms so the progesterone dose is generally kept up to par with the estrogen dose in order to keep the balance. A typical total daily dose of progesterone is between 100mg and 200mg.

Testosterone is added when there are signs of deficiency. This is usually right around menopause as testosterone drops right along with estrogen. However, testosterone is a "wild card" in that it may drop as much as 10 years before or after menopause. I have women start at the low end of the dose range and increase every few weeks until we see the desired effect. A typical total daily dose of testosterone is between 2.5mg and 10mg.

There are several commercial brands of vaginal creams available (e.g. Vagifem, Estrace). These estradiol formulations are bioidentical and are approved. My preferred recommendation is a compounded Estriol vaginal cream. Estriol has a high affinity for vaginal tissue and does a superb job in treatment.

The Progesterone "Pendulum"

Progesterone has an interesting ability to increase *or* to decrease the effects of estrogen, depending on the dose and the blood level achieved. That is at lower doses progesterone will sensitize estrogen receptors and amplify estrogen influence. This is how progesterone relieves estrogen deficient symptoms, especially in the early phases of pre and peri-menopause. At higher doses progesterone begins to antagonize the effects of estrogen. For example, too high a level of progesterone can cause hot flashes due to overly antagonizing estrogen. In too high amounts, progesterone can also negate estrogens influence on vaginal lubrication, libido, and insulin sensitizing effects. The key, again, is in finding the right balance between progesterone and estrogen.

The Progesterone "Paradox"

Some women will not tolerate a typical dose of progesterone and have a paradoxical response that results in symptoms more typical of estrogen dominance or progesterone deficiency. The symptoms might include anxiousness, even panic feelings, depressed mood, breast tenderness or water retention. In these cases we simply lower the progesterone to an unusually small dose such at 10-20mg total daily dose. There are instances where this paradoxical reaction is associated with a systemic infection by a fungus called Candida.

A Typical Prescription for Starting HRT

This would represent a typical hormone cream prescription for an average sized woman with no unusual menstrual history:

BiEst Cream 2.5mg/ml apply ½ ml 2x/day
Progesterone Cream 100mg/ml apply ½ ml 2x/day
Testosterone Cream 5mg/ml apply ½ ml 2x/day

After a stable dose was achieved then all three hormones would be mixed into one cream and would be prescribed as:

BiEst / Progesterone / Testosterone Cream 2.5mg / 100mg / 5mg / ml apply ½ ml 2x/day

The same prescription in a sublingual tablet would be written as:

BiEst / Progesterone / Testosterone SL 2.5mg / 100mg / 5mg take ½ tab 2x/day

Women who are in the peri-menopause phase and having withdrawal symptoms such as hot flashes and night sweats often simply increase the HRT until the symptoms settle down. This may only take a few days to weeks.

Women who are not having withdrawal symptoms or whom are experiencing deficiency symptoms may need more time to see the desired effects. Starting doses are usually low and over several months the improvement of deficiency symptoms such as vaginal dryness should indicate they are on a good dose.

The Estriol vaginal cream would be prescribed as:

Estriol vaginal 0.5mg/ml apply 1 ml vaginally at bedtime, 1-2x/week

Symptom improvement is usually noted as follows;

- Week 1, reduced anxiety and insomnia
- Week 2, reduced hot flashes, night sweats
- Week 3, improved libido (even prior to starting testosterone)
- Week 4, patient calls to say “I love you”
- Week 5, husband and co-workers start scheduling appointments

Seriously, the improvements are often dramatic such that patients and their family and friends are amazed at how much better they feel!

Early improvements are noted in areas such as mood, sleep and energy. A positive outlook, increases in confidence, motivation, and security are also noted early. Areas that involve a tissue response, such as vaginal dryness, skin hydration, and hair fullness, may take a little longer. Restoration of metabolism, muscle development, lowering of body fat, and changes in body shape normally take months to develop.

Step 6
Making Adjustments – Fine Tune your HRT Dosing

Tips for making minor adjustments to your HRT

- Guidelines for managing symptoms of deficiency or excess HRT
- Simple steps to making HRT adjustments on your own
- When to get follow up testing and what tests to ask for

HRT Dosing Adjustments

There is no "one size fits all" dose with hormone replacement therapy (HRT) and the art of getting the right dose is learning how to balance the hormones. By "reading" the signs of too much or too little of each hormone you can make small dosage adjustments that will fine tune the HRT until it is JUST RIGHT for you.

When using bioidentical hormones in a topical cream you can easily “adjust” the dose by simply applying a little more or a little less of the different components. If you are using a sublingual tablet, then you can adjust the dose by simply biting off a little more or less of the tablets. Symptoms of hormone deficiency are listed previously. Listed below are common symptoms associated with too much of each component in HRT.

Common Symptoms of Too Much Estrogen Replacement:

- Swollen, painful or tender breasts
- Water retention, swelling in hands or feet
- Increased anxiety, irritability and nervousness
- “Reddish” face
- Sleep difficulties
- Weight gain, especially before periods
- Heavy, painful periods
- Migraine headaches, especially before periods

Common Symptoms of Too Much Progesterone Replacement:

- Sedation and excessive sleepiness
- Feeling groggy or “drunk”
- Depression
- Impaired memory and reasoning skills
- Decreased coordination
- Decreased libido
- Urinary Incontinence

- Excess vaginal dryness

Signs and Symptoms of Too Much Testosterone Replacement:

- Facial hair
- Excessive body hair
- Acne
- Oily skin
- Swelling of the feet
- Excessive sex drive
- Excessive aggression or authoritarian attitude
- Excessive muscle development

By learning the "signs" of each hormone you can improve the balance of your HRT.

Once the HRT dose seems right we combine the different components into a single tablet or cream. At this point it is time for testing. Usually the follow up lab testing confirms good levels or leads to very minor adjustments in the HRT dosages.

Step 7
Are We Done Yet?

Learn whether you need to work on other areas in order to be at your best!

- Repeat the "Master Symptom Questionnaire"
- Determine if all systems working well or which ones may need more work

If there are residual symptoms of significance then the sex hormones may need more fine-tuning or there may be other unresolved issues to sort out. Revisit the symptoms of low thyroid or low cortisol and pursuer further work-up for these areas.

Remember that proper functioning of sex hormones is dependent upon good intestinal and liver health. Many symptoms that one might think are sex hormone related, such as fatigue or weight gain, are improved by working on other areas including removing food allergens and treating chronic infections such as Candida.

Once the sex hormones are replaced and/or balanced they should be reviewed and serum levels examined on a yearly basis. They should be continued indefinitely to help prevent disease and maintain quality of life.