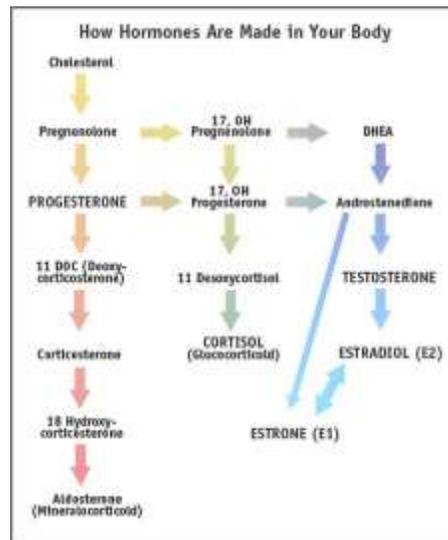


Bio-Identical Hormones

Part 2

Selection, Administration, & Considerations



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Introduction

The subject of hormone therapy is a big one in our modern times. In fact, the endocrine system, which governs the world of hormones, provides many challenges for both the conventional and naturopathic communities. It's nature as a system in constant flux – one that is both setting the stage for health and responding to it can be tricky. One treatment therapy that has emerged as a more “natural” treatment for the ups and downs of the endocrine system is “Bio-Identical Hormone Therapy”. The term Bio-identical is not a marketing term, it is a descriptive term. It describes the biologically identical molecular formula born by Bio-identical hormones. It is a term that makes the important distinction between Bio-identical hormones and non-biologically identical or synthetic hormones. Their popularity in use came about somewhat as a response to the dangers of conventional Hormone replacement therapy or HRT. Bio-Identical Hormone replacement therapy or BHRT has been hailed as a “VERY SAFE” and “NATURAL” alternative to conventional HRT since the composition of the hormones are chemically the same as human hormones. Part 1 of this research work answered some fundamental questions about history, safety, and efficacy when it comes to Bio-identical hormones. To recap: Here are the important initial points to take-away about Bio-identical hormones from Part 1:

- All Bio-identical hormones used are chemically identical to human hormones.
- Some Bio-identical hormones are commercially available and some are available in compounded dosage forms. Compounded products are made at specialty pharmacies in doses that are customized for each client. The dosage can be individualized to a

patient's specific hormonal needs and can only be obtained by prescription from an M.D., D.O., Naturopathic medical doctor or Chiropractor in certain states.

- Bioidentical Estrogens include Estrone, Estradiol, Estriol, 17 β -Estradiol, and Estradiol hemihydrate.
- Bio-identical Progesterone is available, as are Testosterone, Androstenedione, Dihydrotestosterone, and DHEA.
- Over-the-counter or (OTC) Commercial preparations are available of Progesterone, DHEA, Melatonin, Pregnenolone, Estriol, and Estradiol.
- Commercially-available Bio-identical products come in specific strengths that cannot be customized.
- A good majority of hormone balancing can occur with the workhorse and overall balancer of the endocrine system, Progesterone.
- Careful attention and scrutiny to all hormonal products is needed due to the co-opting of the word "natural" in relation to the product's formation and use.
- Semantics matters when describing and detailing ALL hormonal products. Current medical professionals, the lay public, and even researchers use the names of hormones interchangeably. This is both inaccurate and misleading. A very common error is seeing PROGESTERONE, PROGESTOGEN, and PROGESTIN used interchangeably. They are NOT the same thing.

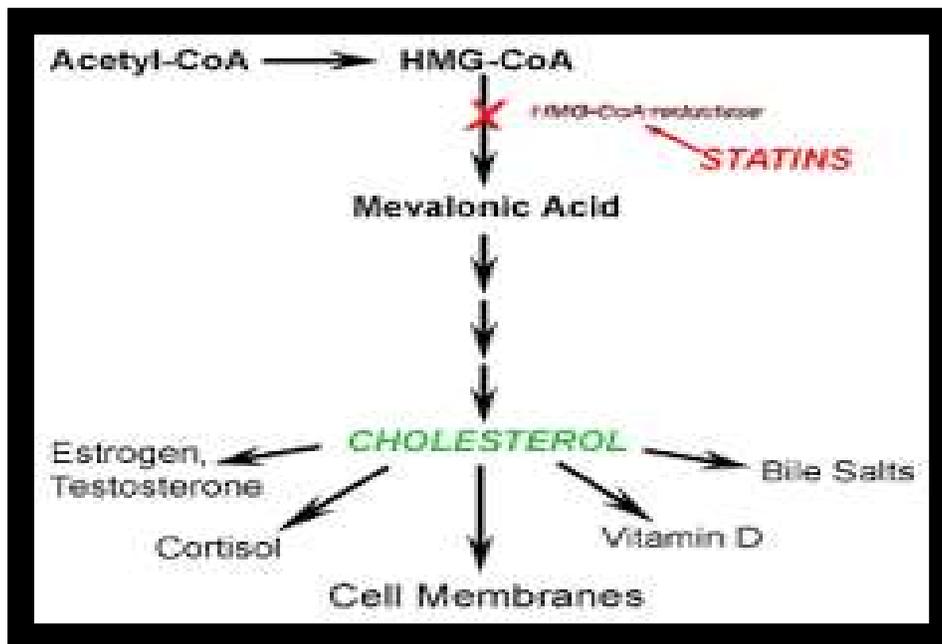
Part 1 of this work gave Traditional Naturopathic practitioners solid assurance that the foothold of time, study, and research exists solidly in the realm of Bio-identical products. The decades of treatment profiles from doctors and litany of research readily available about Bio-identical hormones is very easy to obtain and peruse. It showcases decades of great success that Bio-identical hormones enjoyed with diverse conditions ranging from asthma to Pre-Menstrual Syndrome. The work of pioneering Women's Health champion Dr. Katherina Dalton showcased how Bio-identical Progesterone allowed MANY women to carry babies through to full term instead of suffering miscarriage. Traditional Naturopathic practitioners can rest assured that the foothold of time, study, and research exists solidly in the realm of Bio-identical products. Part 2 of this research work delves deeper into Bio-identical hormones and

answers important questions that Traditional Naturopathic practitioners would need to know in relation to administration, usage, and sourcing of these all-important tools assisting a return to health and balance.

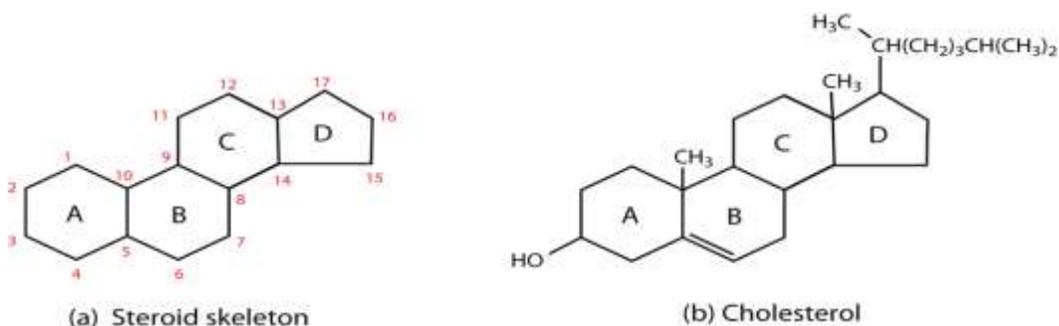
The Cholesterol and Sex Hormone Pathway

Achieving hormonal balance in the human body using Bio-identical products requires a thorough understanding of the synthesis and production of hormones being done by the body everyday. The first step in understanding how many hormones in the body are made is recognizing that adequate CHOLESTEROL must be available for hormone synthesis to occur. This paper focuses on hormones along the cholesterol pathway and champions cholesterol as a protective and formative substance for the body. Not all hormones in the human body are found along the cholesterol pathway but this work will cover the sex hormones that have direct relation to cholesterol levels within the body. (Hormones that are not on the cholesterol pathway include insulin and thyroid hormones but understanding the interaction of the 3 is crucial for understanding how to use Bio-identical hormones). Humans obtain some cholesterol from the foods we eat, but the liver produces the majority of the cholesterol our bodies need. If a person eats too little cholesterol, the body doesn't have the building blocks it needs to manufacture a number of hormones and other products the body needs for optimal functioning. 75% of our cholesterol is made from carbohydrates but the remaining 25% comes from fats and oils. The standard American diet promoting low-fat or no-fat eating works in

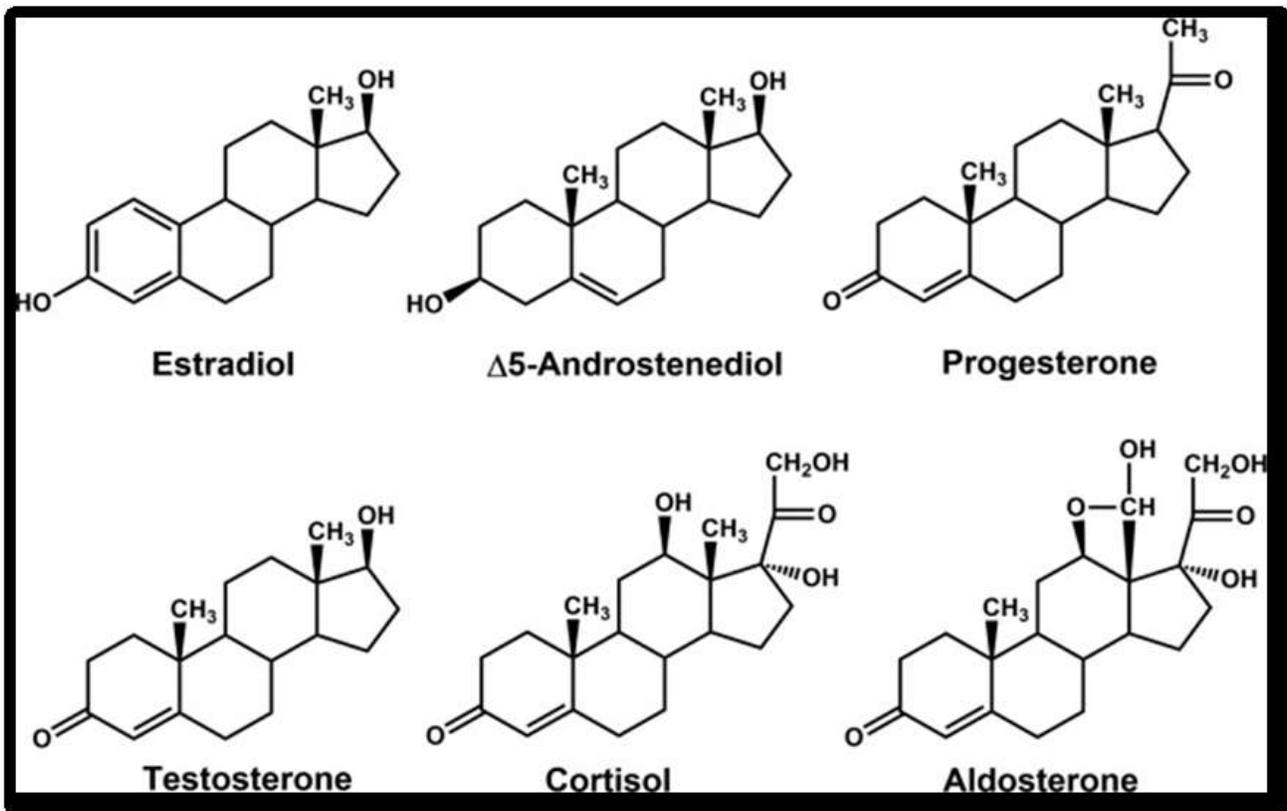
direct opposition to adequate cholesterol production in the body. Though this paper will only cover the hormonal aspects of cholesterol in the body, MANY other biological components depend on the cholesterol pathway to exist. Note the chart below showing the problematic downstream consequences of taking statin drugs – drugs that disable cholesterol production in the body!



To understand the importance of Cholesterol as a foundational substance in the body, note the visual representation of the four rings that make up the chassis of the molecule. These four rings, A-B-C-D characterize all the steroid hormones.

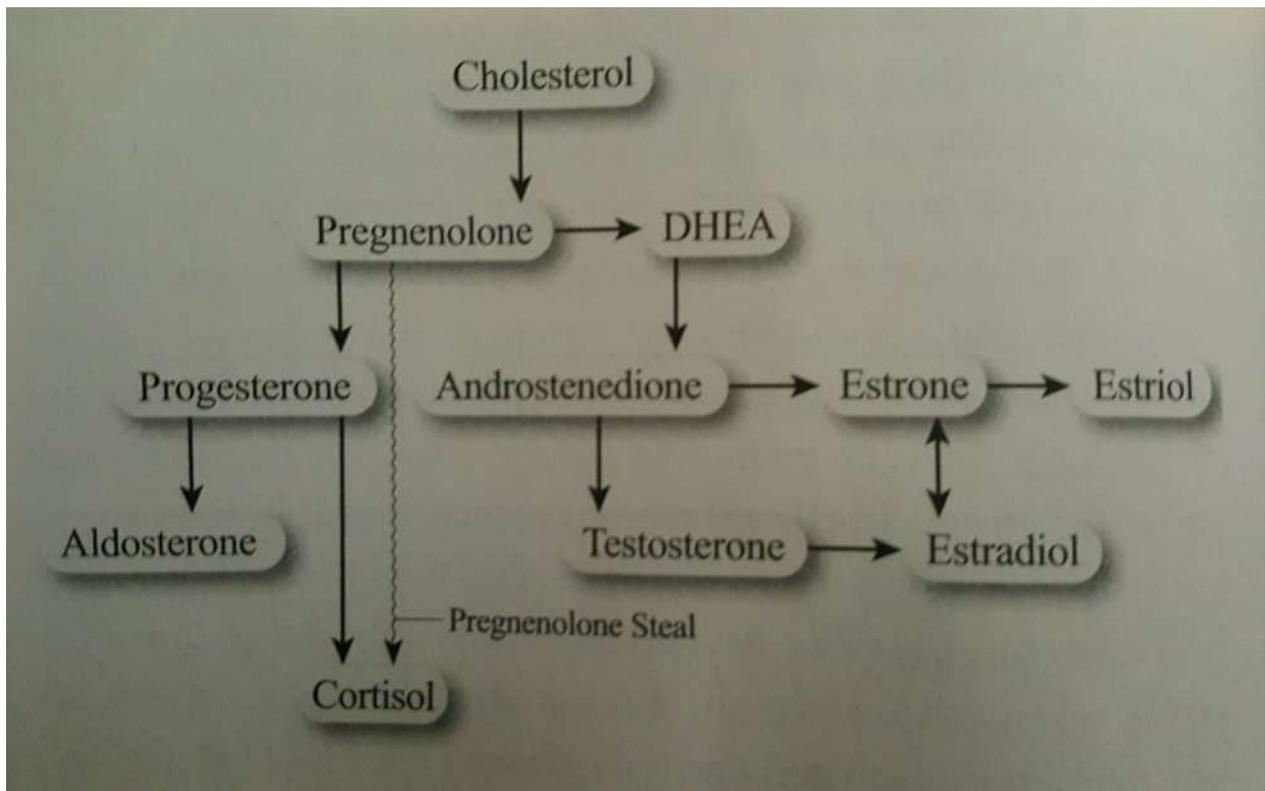


Note the four-ring configuration in the following models:



The first step in the body's manufacture of hormones from cholesterol happens in tiny energy packets called mitochondria found in every cell of the body except red blood cells. From cholesterol, the mitochondria make a hormone called Pregnenolone which is the "mother" hormone from which other hormones are made. Under normal and calm circumstances in the adrenal glands, it can be transformed into either Progesterone or Dehydroepiandrosterone or DHEA. DHEA is a precursor to Testosterone and Estrogen. Progesterone is a precursor to aldosterone and cortisol. (A substance that is the source of another substance is called the precursor). When the body is chronically stressed, it makes more cortisol, stealing excess

Pregnenolone which causes other hormone levels to fall. This process is called the Pregnenolone Steal and showcases clearly the importance of keeping stress levels in balance. In this sort of production method, note that one hormone on the chain is transformed into another active hormone in it's own right – even as it's part of a chain process. The transformation from one hormone to another requires enzymes, which in turn require vitamins and mineral cofactors.



The journey of the cholesterol pathway hits it's stride once the 2 distinct branches following Pregnenolone have been formed. The first pathway is the adrenal DHEA pathway and the other is the gonad/adrenal route. Both pathways lead to metabolic end points with Aldosterone, cortisol, and the estrogens being final stops. With the exception of end point

hormones, all of the steroid hormone molecules are capable of being converted into some other molecule. The determining factors for this to occur are stress, nutritional status, and even the presence of parasites. The fact that the body can do this sort of exchange and conversion with these most important chemical messengers of the body is the reason a practitioner MUST have solid understanding of hormone interaction so it is approached with respect and order. Hormones are powerful and not to be toyed with or approached from a less than knowledgeable standpoint.

What happens symptomatically when the body is out of balance and hormone levels are askew? Here are some of the common imbalances found with this group of hormones:

- High cortisol – Causes a person to feel tired but wired, and prompts the body to store fuel in places it can be used easily, such as at the waist.
- Low cortisol – Causes a person to feel exhausted and drained.
- Low pregnenolone – Causes a person to have trouble finding the right word, anxiety, mild depression, and brain fog.
- Low progesterone – Causes a person to have night sweats, sleeplessness, irregular menstrual cycles, hot flashes, and infertility.
- High estrogen – Causes a person to possibly develop breast tenderness, cysts, fibroids, endometriosis, water retention, erectile dysfunction, and breast cancer.
- Low estrogen – Causes mood and libido to plunge, makes the vagina less moist, joints less flexible, hot flashes, and mental state less focused and alive.
- High testosterone – Causes rogue hairs on the chin, acne, and another reason for infertility.

Specific types of symptoms go with each arena of imbalance – this reality can be used to determine what imbalances a client may be experiencing at any given time. Dr. Joseph Collins, N.D. devised a method of using detailed symptoms lists to help him understand menopause and its variations in his patient population. Those lists led him to detail 12 different types of

menopause. He then created specific supplement regimens and dosing guidelines for each type of menopause. This information guides and rebalance his client's hormonal profiles. A full rendering of the possibilities of hormone imbalance and regulation is true health detective work!

The work of hormones has everything to do with hormone receptor capability and there's a multitude of factors that may affect message reception. Here's just a few situations that often occur with hormone imbalance related to the receptor:

- Assuming there is hormone moving within the body, a symptom is going to occur in the body if the hormone never reaches the receptors designed to accept it. Altered conditions outside the cell alter this passage. Examples of this state are insulin resistance and Progesterone resistance. In the first case excess glucose is the culprit and in the other the culprit is problems among four entities: Progesterone, allopregnenolone (a derivative of Progesterone), and the GABA and serotonin pathways.
- Another issue that can occur in relation to receptor sites is an inadequate amount of receptors to take the hormones up. There are people with genetic abnormalities that lack certain types of receptors in their cells. There is a medical case study of a woman with normal Progesterone levels that lacked Progesterone receptors. This proved to be a highly unfortunate condition, in that she died from breast cancer in her 20's due to being unable to uptake Progesterone.

- Another receptor condition that can exist is the receptor site being occupied by an alternate hormone or molecule. The perfect example of this is cortisol and Progesterone. Either one can occupy a Progesterone receptor site and thus can compete throughout the body for these sites. There are Progesterone receptor sites in osteoblasts, for example, the bone building cells in bone. The message of Progesterone to osteoblasts is to stimulate them to make a new bone whereas the message of cortisol is to inhibit them from making new bone. Thus, the former prevents osteoporosis and the latter can cause osteoporosis. Excess cortisol blocks Progesterone's action and can cause a Progesterone deficiency. (Part 1 of this paper showcased early champions of Bio-identical Progesterone using it to address bone health in women!).
- Arguably, one of the biggest problems with hormone receptor sites is their nature to be accepting. The womblike shape of the receptor allows many different molecules that are only "similar" in shape to enter and bind with the receptor. In the words of some scientists, the hormone receptor site has a "wobble" - meaning it is flexible and accommodating. Scientists assign a degree of "binding affinity" to a hormone receptor and this dictates how much more likely it is that the hormone or ligand will stay in the site long enough to have its action follow. The problem with hormone receptor sites is that even if there's a hormone with high binding affinity near the receptor, the presence of LOTS of other substances with lower binding affinities can interfere with the proper hormone settling into the site. Many hormone receptors found in the nucleus of a cell

have lots of flexibility to accept a wide range of compounds. Once a receptor site has been bound, a message or signal is going to be sent out from that cell. If the compound bound to a receptor site is not the one meant for that site, the outgoing message can act much like a virus that has been placed into a computer to disrupt it's functioning! This compound may cause the cell to send an altered message, a contradictory message, a destructive message, or may cause the cell to shut down and send nothing. Traditional Naturopathic practitioners can address cell receptor site blockage with essential oils. These powerful oils can help clear blocked receptors. This therapy helps the body stay in it's desired state of homeostasis.

Bio-Identical Progesterone – the Ultimate Hormone Balancer

Dr. John Lee, M.D. coined the term “Estrogen Dominance” and it has proven to be an astounding key to unlocking hormone imbalance by providing a better way to think about it, describe it, frame it, and most importantly ADDRESS IT. He is known as an early champion of looking at Estrogen and all the so-called “sex hormones” in the body in terms of RATIO FIRST THEN LEVEL if needed. Estrogen dominance is a condition of a person having deficient, normal, or excessive estrogen but little or no Progesterone to balance it's effects in the body. Dr. Lee's introduction to Bio-identical Progesterone came about because of a biochemist named Dr. Ray Peat – another early champion of Bio-identical Progesterone. Dr. Lee had a chance meeting of Dr. Peat at a conference in which they were both presenting. After his presentation, Dr. Lee

heard a lecture by Dr. Ray Peat and his topic was “Bio-identical Progesterone and the dangers of prescribing unopposed Estrogen”. Dr. Lee was astounded with the information and connected with him immediately. Dr. Lee then began researching Bio-identical hormones, and in particular, PROGESTERONE. His research and dedication meant great health success in his patient population. After years of treating female patients with unopposed synthetic Estrogen and seeing them suffer water retention, headaches, tender breasts, and weight gain he knew there had to be a better option. His turning point came when he was confronted with patients he had known for years beginning to suffer from progressive osteoporosis. These patients could not take Estrogen – his only suggested therapy at the time - because of a history of breast cancer, uterine cancer, diabetes, gallbladder disease, and a host of other problems. As he got more confident with his research into Bio-identical Progesterone a fortuitous event occurred. Bone density scans became available and doctors could assess in detail the condition of patients’ bones. Up to that point, Dr. Lee’s research and study showed clearly that Progesterone was the answer for his suffering patients. He decided it was time to start administering a Bio-identical Progesterone cream to his patient population. To his delight, bone density scans taken before and after using the cream showed SIGNIFICANT INCREASE in bone density with his patients on the product. The results were far higher than his patients on Estrogen alone and of course even more than those who took nothing. Many of his patients on the cream alone also showcased a stabilizing of their bones – certainly a great improvement from progressive deterioration. This same patient group also started reporting that one

condition after another had improved since using the cream. Backaches went away, sleep improved, energy levels went up, weight loss happened more easily, skin was less dry and wrinkled, and libido was revived. Among those with a history of cancer, none developed any recurrence or late metastases.

As Dr. Lee began to work intensively with Bio-identical Progesterone, he started taking apart the inner workings of exactly what Progesterone does in the body and what “balance” really means when it comes to hormones. He noted first-hand what dosing levels brought about positive changes and what other sorts of factors played into the supplementing process. After years of working with patients, he began to develop some fundamental teachings. His most important tenet provided the lasting legacy of his work. This legacy is one that Naturopathic and integrative practitioners have absorbed and used in their own arenas. Dr. Lee’s most important and fundamental tenet in regards to Estrogen and Progesterone was that health would be achieved when the two hormones were IN BALANCE, period. He found that a healthy ratio between Estradiol (the strongest of the 3 main Estrogen sisters) and Progesterone is 1:100-200. This means that Progesterone concentrations, as tested in saliva, should be 100-200 times greater than Estradiol for Progesterone to act as a protection against unopposed Estrogen. This then, would set the stage for good health and balance. He was correct but this idea was RADICAL for the conventional medical profession of Dr. Lee’s time. Conventional thinking of the time looked at levels of Estrogen from a patient’s test and then

responded with an Estrogen prescription. There was little to no thought of incorporating other hormones or looking at ratios. Traditional Naturopathic practitioners should familiarize themselves with this disturbing reality of how Estrogen prescribing was done in the past and how it's often done to this day. Estrogen is suggested and prescribed to patients whether their levels are **low or high** based on what the "normal" levels are of the time. (Yes, that's correct, even with a high level of Estrogen many times the standard of care is to prescribe an Estrogen product). There's certainly danger in giving a person with high estrogen levels MORE ESTROGEN. That's equally the case for someone in a state of Estrogen Dominance. Part 1 of this work gave examples of the many unfortunate people who found out first-hand the dangers of Estrogen therapy. Thankfully, Dr. Lee had a holistic framework and instead of focusing on Estrogen levels put the focus on Progesterone! If all available Estrogen in the body was matched with it's appropriate counterpart, for this arena - at least - balance would rule.

Estrogen and Progesterone have differing effects in the body and Traditional Naturopathic practitioners considering Bio-identical hormones MUST internalize the many aspects of what these two hormones can do in the body. Below is a chart comparing their actions in the human body.

Comparison of Estrogen and Progesterone effects in the body

Estrogen

Stimulates uterine lining cell growth
Stimulates breast cell growth
Adds to body fat
Promotes water/salt retention

Progesterone

Stabilizes uterine lining cell growth
Stabilizes breast cell growth
Helps body burn fat as fuel
Diuretic

Promotes depression	Antidepressant
Causes headaches	Reduces head pains
Anti-thyroid hormone	Pro-thyroid hormone
Promotes blood clotting	Stabilizes blood clotting
Diminishes sex drive	Increases sex drive
Upsets blood sugar balance	Stabilizes blood sugar
Anti-zinc and pro-copper in body	Stabilizes zinc-copper balance in the body
Lowers cell oxygen levels	Normalizes cell oxygen levels
Raises risk of uterine cancer	Prevents uterine cancer
Raises risk of breast cancer	Helps prevent breast cancer
Anti-bone building(restrains osteoclasts)	Pro-bone building (stimulates osteoblasts)
Antivascular reduces blood vessel tone	Provascular restores tone, vasodilator
Increases risk of prostate cancer	Decreases risk prostate cancer
Creates progesterone receptors	Increases sensitivity of estrogen receptors
Increases risk of gall bladder disease	Prevents coronary artery spasm and arterial plaque
Increases brain cell excitability	Improves sleep disorders
May cause panic attacks	*Raises body temperature
Estriol improves urinary tract health	*Prevents yeast (candida) infections/high dose
Relieves night sweats	

It is very easy to see from this chart how Estrogen acts in the body and the problems that can possibly arise from having a condition of too much circulating Estrogen in the system. Estrogen's general capability in the human body is to focus on cell growth and proliferation. Estrogen allows an influx of water and sodium into the cell, affecting aldosterone production leading to water retention and hypertension. Estrogen causes intracellular hypoxia (oxygen deficiency), promotes histamine release, and thickens bile. Is it any surprise that blood clots, strokes, thyroid issues, cancers, and even gall bladder disease were found in people taking synthetic Estrogens since it alone was the most championed therapy of the conventional medical establishment? Synthetic Estrogens provide a two-fold problem: They load the body with too much Estrogen AND do so with a synthetic format that the body can't metabolize in

it's entirety. In conditions of people already in a state of Estrogen dominance this would create a disaster situation. Part 1 of this work detailed one such disaster that came to pass in the Women's Health Initiative Study. That study was abruptly cut short after five years (three years early) due to the findings of greater risk of invasive breast cancer, heart disease, and strokes among women using PremPro, a popular hormone treatment of at the time. (PremPro is a synthetic Estrogen and Progesterone! It's still in use today.) The panic that followed that study and subsequent legal action are the reason all hormone therapies and products prescribed by M.D.'s and D.O.'s MUST be dispensed with a warning label to this day.

As conventional doctors moved to treatments on the Bio-identical platform instead of synthetic options, various forms of Estrogen like Estriol, a weak estrogen, provided some balance in prescribing. Curiously though, pharmaceutical companies began creating hybrid products like Bio-identical Estriol mixed with synthetic Progesterone – a product totally defeating the purpose of using Bio-identical products in the first place. Luckily, common sense prevailed among practitioners interested entirely in Bio-identical hormones. For them, balance was always key. These practitioners found that because so many people were in a condition of Estrogen dominance, the best response was Bio-identical Progesterone FIRST and then considerations of other additions. The next logical question to be asked is how people get into a state of Estrogen dominance? In this day and age, it's far too easy. Chemical inputs are often the culprit, but there are other culprits such as improper diet, birth control pills, and obesity. Parasites and chronic infection are lesser known culprits but ones that do exist. The next

portion of this work will cover the differential factors that create a state of Estrogen dominance in the body. Traditional Naturopathic practitioners will benefit from running the entire differential on a client and assessing which culprit may be to blame. Unfortunately, more than one can be at work.

Estrogen Dominance and Differential Factors that Inhibit Progesterone

Estrogen dominance can be identified by symptom and it's often easy to spot. These effects in the body that are usually far-reaching and often chronic in condition. Estrogen dominance has similar characteristics to MANY other states of imbalance. Because it's such a fundamental cellular-level imbalance, it warrants scrutiny and great consideration when trying to determine root cause of any imbalanced state. Traditional Naturopathic teachings state that addressing the ROOT (cause) will often fix the BRANCH (symptom). Following this truth, Estrogen dominance should **always** be considered a possible root cause when working to untangle EVERY client's health. The exact degree of Estrogen imbalance that a client is carrying can be gauged precisely with a blood, urine, or saliva test. (More information on laboratory testing follows in this work). However, Estrogen dominance shows itself in a myriad of physical symptoms. Taking careful note of ALL a client's symptoms can set the stage for the proper placement of Estrogen dominance as a root cause for imbalance. Common signs of Estrogen overload are:

Bloating, breast swelling, depression, fat deposition on hips and thighs, hypothyroid symptoms, mood swings, irregular periods, periods occasionally heavy, decreased libido, sugar cravings, tiredness, uterine fibroids, water retention, weight gain, accelerated aging, allergy symptoms, autoimmune disorders, copper excess, dry eyes, gall bladder disease, hair loss, hypoglycemia, infertility, insomnia, irritability, magnesium deficiency, PMS, zinc deficiency, enlarged prostate.

There are 11 differentials that can be examined when working to assess Estrogen Dominance or Progesterone inhibition in a client. They are as follows:

1. The Stress and Cortisol cycle

When the body is chronically stressed, it makes more cortisol, stealing excess Pregnenolone. This bypasses the all-important Progesterone step. Moving directly from Pregnenolone to cortisol causes all other hormone levels to fall. This process is called the Pregnenolone Steal and showcases the importance of keeping stress levels in balance. Naturopathic practitioners should carefully assess a client's stress levels and ability to handle stressful situations. Of course best practice suggestions to reduce stress would be wise.

2. Iatrogenic (Doctor-caused)

Iatrogenic illness is brought on by medical examination or treatment. In relation to Estrogen dominance, there are many conventional drugs and treatments that create a situation of Estrogen dominance. Traditional Naturopathic practitioners should ask a client about their history with the following treatments, as they tip the scales of Estrogen in the body: Birth control pills and Conventional HRT. Practitioners should examine the health history of all female clients dating back to their teenage years, as this is often the time birth control pills may have been first prescribed. This unfortunate occurrence early in a woman's life can tip the balance of Estrogen negatively. This can manifest into diseases like gall bladder disease, hypothyroidism, and even cancer later in life.

3. Diet and Nutritional factors

Estrogen dominance in a good majority of our modern population comes from improper food choices. This often starts before we are even born. The relationship of food to hormones is very clear. Adequate amounts of the macronutrients Protein, Fat, and Carbohydrates must be available for the body to make and maintain hormonal balance.

The body makes the best use of the three when they are from high-quality, organic sources. Excess protein, lack of quality fats, non-organic meats/dairy/vegetables, excess processed foods, excess alcohol/sugars/coffee, and low-fiber foods ALL generate excess Estrogen in the body. Specific nutrients to look at include Vitamin C and E. Vitamin C at doses of 750 mg/day has been shown to raise Progesterone in women with both low Progesterone and luteal phase defect. Vitamin E is of particular concern for Estrogen balancing. New research has shown that people with metabolic syndrome need significantly more vitamin E. This could be a serious public health concern in light of the fact that millions of people who have this condition have it related to obesity. A study just published in the American Journal of Clinical Nutrition made it clear that conventional tests to measure vitamin E levels in the blood may have limited accuracy compared to tests made in research laboratories, to the point that conventional tests can actually mask an underlying problem. Vitamin E – one of the more difficult micronutrients to obtain by dietary means – is an antioxidant important for cell protection. It also affects gene expression, immune function, aids in repair of wounds and the damage of atherosclerosis, is important for vision and neurologic function, and largely prevents fat from going rancid. Vitamin E is commonly used to assist women with hot flashes and it's success is generally attributed to it's ability to regulate Estrogen. As it relates to Estrogen dominance, Vitamin E acts in the body to increase the ratio of Estriol to Estradiol and Estrone. Estriol is the safest of the Estrogen sisters! Estriol is a weak estrogen and it interferes with Estradiol binding to ER alpha receptor sites. An additional note for women is that low Magnesium leads to excess Estrogen in pre and post menopausal women. Naturopathic practitioners should work carefully with clients to optimize their diets based on quality, quantity, client blood type, and even assess if a change in relationship to food is needed for a client. Nutrient density is the goal.

4. Environmental Xenoestrogens

Xenoestrogens are chemicals that can mimic estrogen. (Xeno means foreign). These are chemicals that have an estrogenlike reaction in the body. It's important for Naturopathic practitioners to recall that Estrogen receptor sites are very accommodating and can accept various types of molecules. When these chemicals bind to the receptor sites they can trigger a few different options. They may trigger a particular task, send an altered message for a task, trigger a message that is contradictory to the cell's normal message, or trigger a destructive task. Xenoestrogens are EVERYWHERE in our modern environment. We are exposed to them in our air, water, food, homes, and businesses. Xenoestrogens are found in clothing, medical devices, shower curtains, home renovation materials, paints, plastics, and even personal care products. Traditional Naturopathic training allows us to assist clients with a slow reversal of exposure to these

products plus provides means of enhancing their detoxification and removal from the body.

5. Reduced liver function

Reduced liver function contributes to Estrogen dominance due to its function in helping the body get rid of Estrogen. The liver inactivates Estrogen during Phase 1 and Phase 2 of the detoxification cycle, through hydroxylation and conjugation. If the liver is too busy struggling with overconsumption of alcohol, a deficiency of B vitamins, or trying to detoxify drugs and other pollutants, it may not be able to breakdown Estrogen through either one of the phases. This will then inhibit its excretion via bile, urine, or the bowel. This excess Estrogen will then recirculate into the body. Naturopathic suggestions that enhance liver function and pay attention to a diet that removes excess burden on the organ will best enhance the liver capability of a client.

6. Obesity

Obesity has a direct connection to Estrogen dominance. Current statistics cite 66% of adults in the United States are overweight or obese. Fat cells MAKE THEIR OWN ESTROGEN from circulating adrenal hormones. Men and women with excess fat have more circulating Estrogen. Obesity is associated with elevated levels of Testosterone as well as Estrogen. There is a vicious cycle of Estrogen dominance related to type 2 diabetes. This form of diabetes involves insulin and its ability to regulate blood sugar. Excess weight and lack of exercise can lead to high levels of insulin. Cells that get too much insulin can become resistant to it. Chronically high insulin increases Estrogen. Estrone, specifically, increases the cell's resistance to insulin. (Estrone is considered the most cancer-forming of the Estrogens!). The cycle then becomes: higher insulin creates higher estrogen, which can lead to higher insulin and insulin resistance, which tends to make a person gain weight, which leads to making more estrogen. There is an important differential for perimenopausal women that involves a change in Estrogen production location. Before menopause, women make estrogen mostly in the ovaries. After menopause, women make estrogen mostly in the fat tissues. A common symptom women cite when in perimenopause is weight gain. This biological response occurs to allow for roughly 5 to 10 pounds weight gain as a response to shifting Estrogen production location in the body. Weight gain that exceeds this general amount will place excess amounts of Estrogen into the body, more than is needed to accommodate shifting production location. This can exacerbate Estrogen dominance for that population. Traditional Naturopathic practitioners should consider weight loss suggestions that rework the fat-to-muscle ratio. High intensity interval training (HIIT) combined with intermittent fasting is currently an effective strategy. Both of these

strategies effectively boost the body's fat burning capabilities; together they virtually force the body to shed fat. HIIT workouts have been shown to burn more calories than traditional workouts and burn more body fat in less time. Beginning suggestions would include being more active by walking 30 minutes a day.

7. Constipation and impaired Gut health

Constipation is a direct driver of Estrogen dominance due to the bowel being a direct removal system for Estrogen from the body. The hydroxylation and conjugation process of the liver prepares excess Estrogen to be removed from the body. If this excess Estrogen gets to the bowel and encounters constipation of any sort, the gut will REABSORB Estrogen. Naturopathic practitioners can most assist a client with Estrogen Dominance by assuring this method of elimination is optimal. Suggestions that include high amounts of dietary fiber or supplement will insure excess Estrogen is captured and removed as the body sees fit. Consideration should also be given to the balance of gut bacteria in terms of building the "good" bacteria that will keep others in balance.

8. Age

Aging can be an important indicator of Estrogen dominance. Estrogen dominance can certainly strike anyone at any age, but getting older has some specific considerations to look for. As both men and women age, the need for cholesterol will slowly rise to accommodate increased need for hormones of the body as well as neurotransmitters. Increased demand for hormones on the cholesterol pathway always generates a possibility of flux as it relates to Estrogen dominance. As women enter perimenopause and even menopause, fluctuating levels of Estrogen production will almost certainly generate Estrogen imbalance. Naturopathic suggestions for this population MUST focus on adequate Progesterone production, exercise, stress regulation, and mind/body/spirit strategies that acknowledge and bring joy for this change of life status.

- The next 3 differentials relate directly to the Cholesterol pathway. Estrogen dominance has direct relation to this pathway due to the presence of excess cholesterol responding to external slights the body is trying to address and mitigate. Excess cholesterol production being directed towards all the following situations in the body means **reduced** production of ALL other hormones along the pathway. Progesterone production will inevitably fall and allow Estrogen to proliferate without balance. This creates a very precarious situation as each one of these differentials has downstream consequence that could also be negative.

9. High cholesterol due to heavy metal toxicity

Researchers from the Japanese National Institute of Agrobiological Sciences think they may have found an interesting point in the Cholesterol equation. They discovered that small quantities of lead caused elevated serum cholesterol in animals. In their experiments they found that lead induces the genes responsible for creating the liver enzymes that produce cholesterol. They also found that lead suppresses the gene responsible for the production of a liver enzyme that breaks down and destroys cholesterol. With cholesterol production “turned on” and cholesterol breakdown “turned off” by lead, the animals’ serum cholesterol increased significantly. This showcases clearly that cholesterol is serving as a protective measure and responding to the slight of the heavy metal. The lead/cholesterol connection hasn’t been proven by research on humans yet, but it does showcase observations that Naturopaths and holistic doctors have made over the years about heavy metal exposures. Holistic doctors who do chelation therapy (a process that removes lead and other toxic metals from the body) have noted that cholesterol levels often drop after chelation.

10. High cholesterol due to H. Pylori infection

H. pylori infects one third of Americans, often causing gastritis and peptic ulcers. It costs \$10 billion annually in conventional medical treatments of all sorts. Conventional therapy recommends antibiotics but antibiotic-resistance, often leading to treatment failures, is becoming increasingly common. A study published in the June 2011 issue of the journal Antimicrobial Agents and Chemotherapy made a fascinating discovery about H. pylori and it’s ability to adapt and proliferate. In the study, the investigators grew H. pylori in the presence or absence of cholesterol, and then treated the bacteria with different classes and concentrations of antibiotics, comparing the populations of surviving bacteria. “We found that H. pylori grown with cholesterol displayed a very dramatic increase in resistance to many antibiotics, bismuth, and to LL-37,” says McGee one of the study authors. McGee goes on to state that “There are already data showing that H. pylori-infected patients have elevated serum cholesterol levels, suggesting the bacteria manipulates the human host to produce more cholesterol”. Traditional Naturopathic practitioners must take note that this research would suggest to the conventional medical world that patients would benefit from taking a statin drug to address this adaption of the bacteria. Naturopathic suggestions for H. pylori would be well warranted in lieu of doing anything to further disrupt the cholesterol pathway and allow Estrogen dominance to set in.

11. High cholesterol due to gum disease, Hepatitis C, Herpes virus, Dengue virus, Epstein Barr virus, and parasites such as Plasmodium, Giardia, Toxoplasma, Cryptosporidium, Leishmania, Trypanosoma, Ascaris, Entamoeba, Schistosoma, Intestinal worms, Ancylostoma, Filaria, and Hymenolepis

The presence of disease, viruses, and parasites in the human body is a research arena with clear application to Estrogen dominance. Fascinating research into cholesterol levels that skyrocket when one of these conditions has set in abounds. The relationship of serum cholesterol levels in people infected with parasites and viruses has drawn the attention of various workers and then of course various researchers. Since it has been shown in in-vitro studies that parasites like Giardia and Entamoeba can grow in lipid (fat) rich media in the absence of serum, researchers are looking to discover what mechanism allows them do this. The questions researchers are asking include:

- What is the relation of cholesterol synthesis in the liver and the liver being a major extraintestinal site of infection with Entamoeba histolytica?
- What is the role of cholesterol in enhancing virulence and pathogenicity of E. histolytica and does cholesterol help in cyst formation?
- Entamoeba, Giardia and trichomonads lack mitochondria which synthesize cholesterol yet these parasites have developed unique metabolic pathways that allow them to survive and multiply by scavenging nutrients from the host! How is this accomplished?

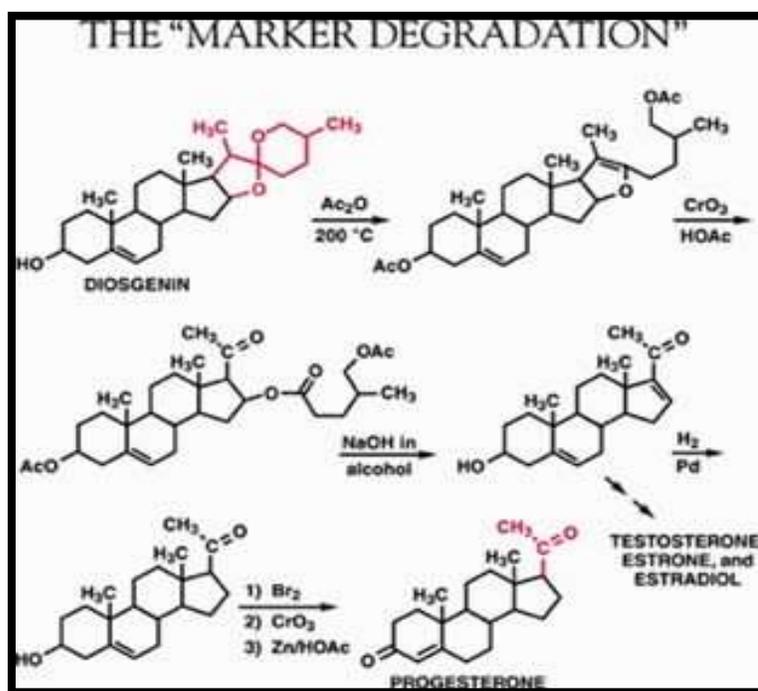
All available and current evidence suggests that parasites are able to remodel/metabolize host lipids/cholesterol for their growth and generate their own phospholipid membrane. Traditional Naturopathic teachings recognize the pathogenicity of parasites and provide ample therapies to address their presence. Doing so will allow the cholesterol pathway to adjust itself back to focus on synthesis of hormones favorable to hormone balance.

How to choose Quality Bio-Identical Progesterone products

Bio-identical Progesterone has to be made in a modern laboratory. (The human body CANNOT convert any phytosterol into Progesterone in the body). The manufacture of Progesterone starts with a plant that has adequate levels of phytosterol to extract and use.

There are over 250 different types of phytosterols that have been found in plants. Plants such as the soy bean, Dioscorea species of yam, fenugreek, sisal, calabar bean, certain lily species, yucca, some solanum species, maize, and a host of others contain phytosterols. As plant sterols have a similar molecular structure to cholesterol, they can be used as starting points for the synthesis of Progesterone. The phytosterols in plants have no bond in the A-ring of the molecule and Progesterone has one. This is why the molecule must be changed in the laboratory setting. The first steps of Progesterone synthesis involve soaking plant material in acid, usually hydrochloric or sulfuric acid. This broth soaks in containers for hours under a hood to allow fermentation to begin. Then the mixture is placed into glassware and specialized equipment to achieve a reflux state. (Reflux is a method of applying constant heat to a mixture without losing any of the liquid to evaporation. The vessel containing the chemical mixture is placed in a second vessel filled with water or oil. It is then attached to a condenser, which cools vapors back into liquid). A solution of ethanol, ammonium sulfate and petrol is then added to the broth and stirred. The sterol separates from the rest and is found in the top fraction. The solute is then evaporated. (In order to get cleaner results, chemists dissolve the solid again and crystallize it subsequently. This re-crystallization represents a fundamental method to obtain the cleanest results.) The separation of the specific sterol needed occurs using HPLC (High Pressure Liquid Chromatography) or GC (gas chromatography). Once separation is complete the sterol is used to form the exact Progesterone molecule the human body produces. The chemistry behind the production of Progesterone is called Marker's

structure after the chemist who discovered it. In Marker's structure, the side chain part of the molecule (the red part of the formula in the picture below) is chemically reactive because two oxygen atoms are connected to the same carbon atom. Using this reactivity, Marker invented a chemical reaction sequence that removed most of the atoms in the side chain. What remained duplicated the side chain of Progesterone. (Chemists call such processes "degradations.") Subsequent chemical modification of the steroid ring system then yielded Progesterone itself.



Bio-identical Progesterone can be made in a modern laboratory by a qualified chemist with the appropriate and fairly expensive equipment. Laboratories that produce Progesterone have the option of having their Progesterone USP certified. The term "USP" refers to the grade or purity of the product and is the shortened form of the term "United States Pharmacopoeia".

There are three different grades of raw materials used in products: “USP pharmaceutical grade”, “Food grade”, for human consumption and “feed grade” that is for animal consumption. The difference between grades is one of quality and purity. A substance that is labeled USP pharmaceutical grade will be of the highest quality and purity between the 3 categories. USP Reference Standards are established through a collaborative quality testing process that involves at least three independent labs. USP certification guarantees four things:

- The product contains the USP ingredient listed on the label, in the declared potency and amount.
- The USP ingredient does not contain harmful levels of specified contaminants.
- The USP ingredient will break down and release into the body within a specified amount of time.
- The USP ingredient has been made using safe, sanitary and well-controlled manufacturing practices according to FDA and USP guidelines.
- **Traditional Naturopathic practitioners should consider the value of ALWAYS seeking out Bio-identical products clearly labeled to contain USP Progesterone!**

There are two common plants currently used to make Bio-identical Progesterone: SOY and WILD YAM. The sterol is extracted from the plants and then synthesized as this research paper detailed. Traditional Naturopathic practitioners should note the concern that often comes up regarding soy and its estrogenic capabilities. Many Progesterone creams currently use soy in their formulations. On a molecular level, there is NO POSSIBILITY of the sterol extracted from soy having estrogenic capability in the human body. There is NO TRACE of any soy or any molecule with any estrogenic capability in the sterol that's extracted from soy. Diosgenin, which is the only ingredient that's taken from the soy, is what is used to make bio-identical Progesterone. If naturopathic clients have no interest or understanding of the chemistry

involved with the process or still have concerns about using a soy product, many Bio-identical creams and products now use wild yam for synthesis of Progesterone.

The question of how much Bio-identical Progesterone to use is based on client need and symptom severity. Under normal circumstances, the human body produces about 25mg of Progesterone per day. Clients with a small amount of symptoms would aim for that amount. Clients with severe symptoms may need to be in the range of 100mg per day and higher. Due to it's safety profile, as much as 600 – 800 mg per day in a cream format is quite safe to use for severe symptoms. It's important that clients keep good record and take notice of how they feel day to day. Bio-identical Progesterone can be monitored entirely by symptom and a solid suggestion to clients would be to stay flexible. Hormones constantly change and Progesterone works almost immediately to establish correction. There are currently many methods of Progesterone administration - pills, sublingual drops, pellets, capsules, oils, and creams. They all have some validity and will often work for clients but the method that is considered superior is transdermal cream. The Progesterone that is applied to the skin passes through it and into the layer of fat beneath it known as subcutaneous fat. The more Progesterone deficient a person is, the more readily it's absorbed. Although transdermal Progesterone given shows up right away in a saliva hormone test, it can take up to as much as three months to show up as higher levels in blood tests. This gradual release is the only dosing method that approximates the natural physiologic release of the hormone from the body's systems. The cream should be applied in varying places on the body DAILY to enhance absorption and

reduce the possibility of the body getting used to the same administration site. Practitioners should take note that it's very easy to obtain blood, urine, and saliva tests both from conventional doctors and direct-to-consumer options when precise levels are desired. ZRT laboratory, www.LabTestsOnline.org, www.DirectLabs.com, and www.WalkInLab.com are great places to start to obtain important levels of the sex hormones and others along the cholesterol pathway. Traditional Naturopathic practitioners should always suggest clients request COMPLETE hormone panels and skip ones that only offer a handful of hormones.

The following is a list of currently available excellent Bio-identical Progesterone creams for practitioners to investigate and determine the best fit for a client.

- NatPro – available at <http://www.organicproducts-llc.com/natpro-airless-dispenser.html>
- Emerita Pro Gest Natural Progesterone Cream
- Life-Flo Progesta-Care Natural Progesterone Body Cream
- Source Naturals Natural Progesterone Cream
- Progesterone cream by Pura Naturalis
- Dr. Randolph's Natural balance cream
- Balance Pro Natural Progesterone Cream for Women
- Serenity for Women Progesterone Cream
- Syngenic Micronized ProCare PE

Other OTC Bio-Identical hormones

and

An herbal Progesterone alternative

Hormones are dynamic and interactive. None of them work independently of the others. Because of this, sometimes clients are leery of any sort of hormone supplement, regardless of it's safety profile. When considering Bio-identical Progesterone, it's important for a practitioner to note that there are herbal alternatives that exist that can stimulate and encourage Progesterone production. There are also other OTC Bio-identical hormones available that can interact with and possibly support all the hormones along the cholesterol pathway. A full discussion of them all is beyond the scope of this paper. Here instead is a brief mention of some common ones practitioners may encounter:

DHEA – DHEA, or Dehydroepiandrosterone is a steroid hormone just like Estrogen and Progesterone. It's made in the adrenal glands and is made in our bodies in greater amounts than any of the other adrenal steroid hormones. DHEA is considered the prehormone to Testosterone and can convert to it when needed. It can also convert to Estrogen so careful attention is needed when considering DHEA. DHEA does not have the ability to trigger the androgen sequence of events in the body - whether building muscle and bone - but it offers raw materials for the intermediate prehormones needed for production of testosterone and estrogen. Daily supplementation should be no more than 5 to 10 mg per day.

Pregnenolone – Pregnenolone is made from cholesterol by mitochondria and is the compound considered a “mother” hormone for others along the cholesterol pathway. It would seem that taking large doses of it, which is very safe and has no long term hormone effect itself, would be a good way to reach hormone balance. Unfortunately, it doesn't work that way. Too many other factors are involved in hormone synthesis

than just the presence of pregnenolone. It does, however, appear to have some benefit on rheumatoid arthritis symptoms. For the population affected with RA, studies have shown that 10 to 50 mg three times daily brings relief. Pregnenolone blocks receptors for the neurotransmitter GABA or gamma-aminobutyric acid. High GABA levels can have the effect of blocking memory and Pregnenolone seems to offset that effect. It also increases brain cell activity.

Progestomend – Progestomend is a formula created by Dr. Joseph Collins, N.D. It is an example of a strong herbal alternative to Bio-identical Progesterone that will support the natural production of Progesterone. It does this by supporting how tissues throughout the body respond to Progesterone. This is accomplished by supporting the function of Progesterone producing glands, and by supporting the function of Progesterone responsive tissues. Many herbs have phytoprogestosterone properties and action that mimics the actions of Progesterone. This product supports healthy adrenal function, a major site of progesterone production. Herbs in this formula include Paeonia lactiflora: (Chinese Peony), Ligusticum wallichii: (Chuan Xiong), Rehmannia glutinosa: (Di Huang), Bupleurum falcatum: (Chinese Thoroughwax), Passiflora incarnata: (Passion Flower), Dioscorea villosa: (Wild yam), Viburnum opulus: (Cramp Bark), Coleus forskohlii: (Indian Coleus), Vitex agnus-castus: (Chasteberry).

Top Naturopathic suggestions for using Bio-identical Progesterone

What makes Bio-identical Progesterone so marvelous and broad in scope? The answer is actually simple: There are receptor sites for Progesterone all over the body and the actions that follow successful docking provide great healing and balance for the body. Remember that hormones convey their message only where and when receptors for them are available.

Exciting research has discovered these receptors all over the body. Below is a chart detailing current knowledge of receptor sites and their actions in the body. It's worth considering Bio-identical Progesterone as adjunct therapy to other naturopathic suggestions even if hormone

balance isn't the desired outcome. Progesterone has application for many conditions outside of its known use in pregnancy. One of the most interesting aspects of Bio-identical hormone research is the discovery by researchers that Bio-identical Progesterone DOES NOT affect the body's recognition of it and alter its production. The common understanding of hormone supplementation is that over time, feedback mechanisms will kick in and the body will limit or discontinue production of a specific hormone due to its current supplementation. According to Dr. Norm Shealy, Bio-identical progesterone is the **only known** replacement hormone that does not suppress or turn off the body's own production of that hormone. This is a key reason he was an early champion of Bio-identical Progesterone. What follows is an exciting and thoughtful list.

<u>Site</u>	<u>Symptoms/Actions Benefitted by Progesterone</u>
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Brain	
Limbic brain	Emotion/psychological symptoms, epilepsy
Hypothalamus	Menstrual cycle, hot flashes, libido
Preoptic area	Libido
Meninges	Headaches
Pituitary	Gonadotropic hormones
Peripheral nerves (Schwann cells)	Myelin sheath repair, MS
Respiratory system	
Nasopharyngeal mucosa	Rhinitis, sore throat, sinusitis, laryngitis, pharyngitis
Lungs	Asthma
Skin	Dryness and thinning, various dermatoses, alopecia
Eyes	Glaucoma
Breast	Breast lesions, cell maturation, and replication rate
Fallopian tubes	Congestion, dysfunction
Uterus (fundus)	Endometrial disease, myomata (tumor of muscle tissue)
Uterus (cervix)	Cervical mucus changes
Testes	Testosterone production
Adrenal glands	Corticosteroid production
Heart and great vessels	Blood flow and oxygenation
Bone	Bone building

General

Anti-inflammatory effects, increases immunoglobulin E (Ig-E) to help prevent sinus, respiratory, and vaginal infections and allergic reactions

There are a few exciting and emerging arenas for the use of Bio-identical Progesterone beyond the above list! Progesterone receptors have been discovered all over the brain and studies have already been showcasing Progesterone to have neuroprotective effects in multiple animal models of brain injury. The efficacy and safety in patients with traumatic brain injury (TBI) remains contentious in the human population though, primarily because of the difficulty of obtaining accurate and consistent study data. While the data in the human population remains inconclusive, the biological models of what Progesterone does in the human body and brain cannot be denied. It may warrant use in an emergency situation while planning a trip to the hospital if a situation of head injury occurs. Another exciting arena of discovery is one that suggests Progesterone may play a previously unrecognized role in combating certain nerve diseases by helping to repair and replace the myelin sheath that surrounds nerve fiber. French researchers discovered that Progesterone is synthesized in Schwann cells and can indirectly regulate myelin formation by activating transcription via the classical steroid receptor. Theories are circulating suggesting that Bio-identical Progesterone would be a strong template as a form of hormonal therapy for diseases that result from the loss of myelin around nerves. Experts say it is too early to know if such an approach would have any relevance to multiple sclerosis, a major demyelinating disease. One doctor is already proposing though, that the synthesis and function of Progesterone in the nervous system

shows it to be more than a classic sex hormone. This doctor is advocating for Progesterone to be reclassified as a neurosteroid. Steroid hormones do not always act as sex hormones, particularly when they have local effects near certain sites where they are made. The work indicates that the same compound made in different parts of the body can play totally different roles at different sites!

SUMMARY – PART 1 and 2

This entire work on Bio-identical hormones, Part 1 and 2 gave solid foundational information for a Traditional Naturopathic practitioner to speak from a position of authority about hormones of the body and therapies that have been created for them. Practitioners considering Bio-identical hormones receive from this work a detailed history of both types of hormonal therapy, the politics involved, and the various outcomes of hormone therapy over the years. Bio-identical Progesterone is presented as a solid champion for health and balance. From this work, practitioners have solid reference on proper and available Bio-identical sourcing and know the questions to ask when referencing products. The varied uses of Bio-identical Progesterone provides an exciting and creative way to address the many possibilities of imbalanced health. Special attention to detail, and solid knowledge of hormone pathways will provide the Traditional Naturopathic practitioner confidence and success into the future with Bio-identical hormones.

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