

Natural Progesterone Cream

Information for women on the safe and effective use of the hormone progesterone



LAWLEY

Hormone Solutions

Contents

Natural Progesterone Cream - An Introduction	3
Natural Progesterone - A History	3
Natural Progesterone Deficiency and Estrogen Dominance	5
Natural Progesterone - Treatment Options	9
The Progesterone Deficiency Assessment Questionnaire	23
What Are The Pros And Cons Of Natural Progesterone Treatment Versus Synthetic Progestins?	24
What is The Role of Progesterone in Humans?	26
Are There Side Effects Associated With Using Natural Progesterone?	27
What About Homeopathic and Herbal Treatments?	28
Natural Progesterone Treatments	28
Natural Progesterone for Women – Quick Q & A	31
Suggested Reading	33
Links to Natural Progesterone Information	33
About Lawley Pharmaceuticals	34
Our Mission Statement	34
Completed Clinical Studies	35
Copyright Information	36

Natural Progesterone Cream - An Introduction

A natural progesterone cream contains only the naturally occurring hormone progesterone. Progesterone is a pivotal hormone in the endocrine system of women. Progesterone is vitally important for reproduction, regulation of the menstrual cycle and for providing a balance to the stimulatory effects of estrogens. When women do not produce sufficient progesterone, the resulting changes can severely disrupt the quality of life of those affected. Mood changes, anxiety, depression, weight gain, irregular periods, headache, migraine, infertility, miscarriage, pre-menstrual syndrome (PMS), post-natal depression, endometriosis and polycystic ovarian syndrome (PCOS) are some of the medical conditions associated with reduced progesterone production.

Natural Progesterone - A History

Natural progesterone is a term used to describe the hormone naturally produced by the ovaries of humans and animals. Progesterone is not produced anywhere in the plant kingdom.

Progesterone was discovered and isolated in the early 1930s. Initially, it was obtained from the ovaries of pigs and later from human placentas. Both these methods were expensive and only yielded small quantities of progesterone.

In 1938, an American biochemist named Russell E Marker manufactured progesterone in a laboratory. He did this by converting another substance, diosgenin, into progesterone through a series of chemical changes. Soon after this breakthrough, pharmaceutical companies then took progesterone and changed it again to give progestins, also called progestagens.

These are compounds with actions similar in some respects to progesterone, but not naturally occurring and therefore patentable.

Since the 1940s they have been using soya beans, wild yams and other plants from the tuber family to make progesterone. It is very important to understand soya beans and wild yams DO NOT contain progesterone. Today, progesterone is produced for pharmaceutical purposes in the laboratory with the aid of enzymes. The vast majority of steroid substrate (raw material) for progesterone synthesis is sourced from soya. The soya bean contains the steroid substrate sigmasterol which is converted into progesterone.



In the early 1990s, US medical practitioner Dr John Lee M.D. pioneered and published books on the benefits of natural progesterone to manage menopausal symptoms, pre-menstrual syndrome and breast cancer.

Dr Lee coined the phrase “natural progesterone” to distinguish real progesterone from progestins. This is because natural progesterone has such a dynamic and holistic action on the body whereas progestins

have an extremely limited spectrum of action. Unfortunately, because of the development and controlled evolution of progestins by the pharmaceutical industry, mainstream medicine does not make the important differentiation between natural progesterone and the synthetic progestins. The lack of understanding by mainstream medicine of this basic premise has been the source of great controversy for many years in scientific circles.

Research has shown progesterone is effectively absorbed and utilized by the human body when taken orally in a high dose or when applied as a cream to the skin. It is also effective when used topically in the vagina.

Over-the-counter remedies for hormonal imbalances may contain wild

yam extracts or homeopathic progesterone, but neither of these are pure natural progesterone. Homeopathic progesterone and wild yam creams contain NO progesterone.

The only progesterone oral capsules and progesterone creams made to international pharmaceutical standards are produced by Besins Healthcare and Lawley Pharmaceuticals respectively. These products use high quality pharmaceutical grade natural progesterone guaranteed to provide meaningful amounts of natural progesterone. Compounding pharmacies do not maintain the exceptionally high and rigorous standards of manufacture required to produce pharmaceutical grade products. Therefore, compounded products do not have the same integrity, stability nor efficacy as pharmaceutically manufactured progesterone products.

Natural Progesterone Deficiency and Estrogen Dominance

Menopause is a stage of life all women go through. In clinical terms, it begins when the woman stops ovulating and menstruation has ceased for 12 months. This usually takes place between the ages of 45 to 55. At this time the ovaries, which have been regularly releasing estrogen and progesterone, slow down their production of these hormones.

The hormones estrogen and progesterone have a very close relationship. Estrogen is a stimulatory hormone and natural progesterone tempers the stimulatory effects of estrogen. This effect of natural progesterone on estrogen is summarized in the table below.

Progesterone has its own intrinsic effects upon the body separate to its action on estrogens.

Estrogen Effects	Progesterone Effects
Builds up uterine lining (proliferation)	Maintains uterine lining (secretory)
Stimulates breast tissue	Protects against fibrocysts
Increases body fat	Helps use fat for energy
Salt and fluid retention	Diuretic
Depression, headache/migraine	Anti-depressant
Interferes with thyroid hormone	Facilitates thyroid hormone action
Increases blood clotting	Normalizes blood clotting
Decreases libido	Restores libido
Impairs blood sugar control	Regulates blood sugar levels
Increases risk of endometrial cancer	Protects from endometrial cancer
Increases risk of breast cancer	Probable prevention of breast cancer
Slightly restrains bone loss	Stimulates bone building
Reduces vascular tone	Propagates growth of embryo
	Precursor of corticosteroid production

During the months and years prior to menopause (peri-menopause), estrogen levels remain stable but ovulation becomes spasmodic. As a result, progesterone production is irregular and declines. At menopause, estrogen levels decline and ovulation ceases altogether. This leads to a hormonal imbalance. Estrogen is free to act untempered by the effects of progesterone.

This unbalanced decline in hormonal levels can lead to many women

experiencing a variety of unpleasant symptoms - what Dr John Lee called 'estrogen dominance'. These symptoms include hot flushes, sleep disturbances, poor bladder control, dryness of the vagina, mood swings and irritability. Some women also report weight gain, lack of energy, malaise, forgetfulness, cloudy thoughts, anxiety or panic attacks, sore bones and general aches and pains. Not everyone will experience all of these symptoms; however, even one or two can be difficult to cope with if not addressed adequately. Correcting any imbalance between the hormones estrogen and progesterone, especially the lack of progesterone, will usually rid an individual of many of these symptoms within a few months.

The time before menopause (peri-menopause) can, in many cases, be more distressing than the actual menopause itself. Peri-menopause is commonplace in women in their late thirties and early forties.

These women are still menstruating, but still experience many of the symptoms traditionally reserved for menopausal women. This can create a great deal of anxiety, depression and confusion.



Irregular or shorter intervals between periods, spotting, irregular bleeding and heavy bleeding are all indicators of hormonal imbalance. The long-held medical belief has been these symptoms and feelings are due to estrogen deficiency. It is now better understood that progesterone plays an active role in preventing these changes from occurring prematurely. If there is a menstrual blood flow (regular or irregular), there is plenty of estrogen being produced by the ovaries.

Estrogen is responsible for stimulating growth of the uterine lining. Progesterone holds the uterine lining together. If there is a deficiency of progesterone, the uterine lining breaks down. This leads to irregular and heavy menstruations.

Often peri-menopausal women exhibiting symptoms are treated with the Pill to “stabilize” their hormones. The Pill overrides the natural hormone production in women. It adds estrogen to the peri-menopausal woman's body but fails to address the progesterone deficiency co-existing. This is because the Pill doesn't contain natural progesterone. Often peri-menopausal women who take the Pill find some of their symptoms worsen rather than improve. This is due to the added estrogen of the Pill not being balanced by natural progesterone, resulting in an exacerbation of "estrogen dominant" symptoms.

The progestin in the Pill does not act in the same way as natural progesterone in balancing the effects of estrogen.

The alternative often suggested to women instead of the Pill is hysterectomy (removal of the uterus). This may or may not include removal of the ovaries (oophorectomy).

Hysterectomy makes no difference to the way the estrogen/progesterone balance should be viewed. Hysterectomy will certainly stop irregular bleeds and heavy blood loss, but does nothing to address the underlying problem of estrogen dominance due to progesterone deficiency.

Addressing this basic imbalance is crucial in order to eliminate unwanted peri- and post-menopausal effects, be they natural imbalances or induced imbalances due to estrogen-only supplementation.

In estrogen dominant peri-menopausal and menopausal women, the first line of treatment should always be progesterone unless hot flushes, night sweats and vaginal dryness are a problem. A woman still getting a menstrual bleed (regular or irregular) is producing adequate estrogen. It is the progesterone that is in deficiency. For decades, the medical profession has been influenced by the pharmaceutical industry into

believing women are estrogen-only entities. In the world of profits, progesterone is a nebulous hormone.

The truth is progesterone is produced by the body in quantities a thousand-fold greater than estrogens. Progesterone is a pivotal hormone for the propagation of life and for the production of other hormones, including estrogen, glucocorticoids and corticosteroids. Without progesterone there would be no menstrual cycle or reproduction.

Natural Progesterone - Treatment Options

- Hot flushes and night sweats
- Irregular and heavy menstrual bleeding
- Breast disorders
- Depression and anxiety attacks
- Pre-menstrual syndrome (PMS)
- Post-natal depression
- Infertility
- Vaginal dryness
- Hormone-induced migraine and headache
- Breast cancer
- Endometriosis
- Polycystic ovarian syndrome (PCOS)

Hot Flushes and Night Sweats

Hot flushes and night sweats are probably the most common and distressing problem experienced by menopausal women. These symptoms can last from a few seconds to several minutes and can be accompanied by heavy unabated sweating. When they happen at night they can disturb sleep and cause serious fatigue and depression. The whole menopause management industry began in the late 1950s

when it was discovered hot flushes and night sweats were relieved by taking estrogen.

Estrogen works well to abate these two major symptoms. Estrogen supplementation quickly became the frontline treatment of menopausal symptoms courtesy of the pharmaceutical companies' massive advertising campaigns and has remained so ever since. In the late 1960s, a massive surge in cases of uterine cancer was directly attributed to unopposed estrogen use. In 2002, a study called the Women's Health Initiative (WHI) highlighted a possible link between breast cancer and long-term estrogen use. This tarnished the reputation of estrogen replacement therapy.

Many women find their hot flushes reduce and their night sweats diminish with estrogen supplementation. However, it is common for these symptoms to be replaced by those associated with estrogen dominance: anxiety, depression, palpitations, loss of confidence, mood changes and irritability. This is simply because supplementing estrogen without balancing its effects with natural progesterone increases the underlying hormonal imbalance. Remember, menopause is the time when ovulation ceases. If there is no ovulation there is NO progesterone production. Many women find at menopause supplementing progesterone rather than estrogen improves the estrogen dominant symptoms. As well as providing moderate relief from hot flushes and night sweats, it narrows the imbalance between the hormones.

Irregular and Heavy Menstrual Bleeding

In the United States, 250,000 hysterectomies are performed annually.

Frequently, hysterectomy is the option taken to control irregular or heavy bleeding in pre- and peri-menopausal women. Many women are content to see the end of their periods and hysterectomy appears to be an easy, quick and clean option. However, hysterectomy for irregular and/or heavy bleeding is a medical response to a symptom rather than

the treatment of an underlying cause.

Progesterone's role in a reproductive woman is to hold the uterine lining together during the second half of the menstrual cycle (the luteal phase). Too frequently, natural progesterone treatment is an untried option prior to undergoing hysterectomy. Irregular and/or heavy bleeding in pre- and peri-menopause is more often than not due to insufficient progesterone production.

Using natural progesterone during the luteal phase of the menstrual cycle will usually regulate and control bleeding within two or three months. It is important uncontrolled bleeding be fully investigated by a gynecologist to exclude serious underlying uterine disease.

Hysterectomized women who undergo a surgical menopause (total removal of the ovaries) have historically been given estrogen-only supplementation after surgery. Supplementation of the hormones progesterone and testosterone is largely ignored by mainstream medicine world-wide.

Balance with the natural hormones progesterone, testosterone and estrogen is the only way to fully address surgically induced menopausal symptoms. A three legged stool is useless without all three legs!



Breast Disorders

Breast tenderness, fibrocystic breasts and swollen breasts are all classical symptoms of estrogen dominance. Breast tissue is very responsive to hormone changes. It is particularly sensitive to changes in estrogen levels. When women start using the Pill or commence hormone replacement therapy (HRT) they will often complain of their breasts getting bigger and feeling more tender. Breast tissue proliferates and grows under the influence of estrogen. It is estrogen that stimulates the development of the breasts and reproductive organs during puberty. In a normal,

healthy adult female, the stimulatory effects of estrogen are tempered and balanced by the hormone progesterone. Progesterone is produced once ovulation takes place at around day 12 of the menstrual cycle. Estrogen and progesterone levels peak around day 22 of the menstrual cycle. When a woman does not produce sufficient progesterone, the effects of estrogen on the breast are unopposed and the breast tissue is affected.

This is typified by painful and swollen breasts in the week pre-menstruation. It is a sure sign there is a progesterone deficiency. The addition of progesterone from days 12 -26 of the cycle will balance the estrogen dominance. Resolution of these symptoms is usually maximized in the third month of treatment.

Depression and Anxiety Attacks

During the peri- and early menopausal years, mood swings, anxiety attacks and depressive thoughts are common. Interrupted sleep, loss of libido, body shape changes, crying spells, irritability, low tolerance and feelings of being “old and past it” are further experiences of menopause. Mixed emotions at this time are normal and women need to be reassured they are not “losing their marbles”. These feelings are a reaction to what is happening to the body both physically and hormonally. The emotional swings and physical changes are a reflection of the hormonal revolution occurring within.

Too often antidepressants are routinely prescribed to address “mood disorders”.

While antidepressants certainly have their place in a medical practitioner’s arsenal of treatment options, they are given to treat the symptom and do not address the underlying hormonal problem.

At the time of menopause, as at the times of puberty, pregnancy and child birth, women undergo massive hormonal changes. During these pivotal phases, emotions and feelings towards one’s self and others can be volatile and complex. Hormones govern the way we think,

the way we act and the way we respond. During times of hormonal turbulence, such as menopause, the imbalance between estrogen and progesterone is of primary importance. Addressing this imbalance will go a long way to resolving many of the emotional symptoms associated with menopause. Most antidepressants can assist in the management of the symptoms, but have little effect on estrogen dominance, progesterone insufficiency and menopausal symptoms.

Pre-menstrual Syndrome (PMS)

When a group of symptoms are so variable in their intensity and so widely experienced they cannot be adequately categorized or defined by evidence based medical standards, it is generally labelled as a "syndrome". To add confusion to the defining of the condition, PMS does not affect all women nor is it restricted to certain age groups. The common thread of PMS is the timing of symptoms in relation to menstruation, hence the name.

In healthy reproductive women with regular menstrual cycles, PMS is typified during the eight to ten days pre-menstrually by breast tenderness, mood changes, irritability, fluid retention, headaches and migraines. PMS is a misunderstood and often ignored condition. It can vary from mildly disconcerting, transient symptoms to a severe and debilitating condition greatly affecting a person's quality of life for over a week every month. Symptoms generally disappear at the onset of menstruation. People who have never experienced PMS symptoms often have little empathy or understanding for those actively suffering from the condition. Families and partners of PMS sufferers often have little or no idea how to respond to the mood swings and symptoms of those affected. Mainstream medicine offers little in the way of treatments. It has for decades ignored natural progesterone.

In a normal, healthy adult female the stimulatory effects of estrogen are tempered and balanced by the hormone progesterone. Progesterone is produced once ovulation takes place at around day 12 of the menstrual cycle. Estrogen and progesterone levels peak at around day 22 of the

menstrual cycle and remain high until just before menstruation. After this both hormone levels fall dramatically, the uterine lining sheds and the period commences.

Women who experience PMS usually are under - producers of progesterone or fail to regularly ovulate (anovulation). When a woman does not produce sufficient progesterone the effects of estrogen dominate and pre-menstrual symptoms flourish. Generally, the more sustained the length of time the woman under-produces progesterone, the more severe the PMS becomes. PMS is not restricted to younger women as is commonly considered. Many women date the onset of their PMS to not long after having a second or third child. Hormonally and physically, pregnancy exerts a massive assault on the female body – especially in women who become pregnant for the first time in their mid or late-thirties.

Women who opt for childbirth in their later reproductive years generally do not spring back into shape hormonally (and physically) post-pregnancy. Post-pregnancy, once the menstrual cycle returns, ovulation usually recommences.

It is not unusual for women in their mid to late-thirties with young children to produce less progesterone post-ovulation than women in their twenties. At this age, however, the ovaries are very efficient at estrogen production. Estrogen levels remain high and the platform for estrogen dominance is formed.

PMS, estrogen dominance and progesterone deficiency are integrally linked. The addition of natural progesterone cream from days 12 -26 of the cycle will balance the estrogen dominance. Resolution of the symptoms of PMS is usually maximized in the third or fourth month of treatment, often sooner. In the 1960s, the English physician Dr Katerina Dalton devoted her life to natural progesterone research and its use in the management of PMS. Her work at the time was ridiculed by her peers and yet today it is considered cornerstone work in this neglected area of medicine.

Post-natal Depression

Progesterone is the most pivotal hormone of pregnancy. Progesterone promotes the pregnancy - *pro gestation* - hence the name.

During pregnancy, progesterone levels rise from a non-pregnant daily production rate of about 20mg per day to up to 400mg per day. Estrogens also rise during pregnancy, but not to the same degree as progesterone. The placenta is responsible for the massive increase in progesterone production, and takes over progesterone production from the ovaries at around week 10 of the pregnancy. Progesterone levels are at their greatest during the third trimester of the pregnancy. It is during this time when many women “nest” and “bloom”. Clarity of thought, mental acuity, high energy levels, confidence and zeal typify this period of many women’s pregnancies. With the birth of the child and the passing of the placenta, blood levels of progesterone fall dramatically. Breastfeeding has the natural action of inhibiting ovulation. Progesterone levels remain low until ovulation recommences. The “second day blues” is a common and transient phenomenon to the new mother, but the more lasting and pervading depression that can overcome some women is triggered by the huge hormonal withdrawal that occurs after the birth of a child.



It seems strange nature would engineer such a huge hormonal shift. In the animal kingdom, many females eat the placenta immediately after the birth. Such an action may seem repugnant to humans, but the placenta is highly enriched with progesterone. Mother Nature may be assisting animals more than we realize. It is logical the addition of natural progesterone post-partum to women who experience post-natal depression will assist in relieving symptoms. Natural progesterone does not interfere with breast milk production and offers a far more reassuring treatment than antidepressants to the new mother. High dose natural progesterone cream treatment combined

with professional counseling is usually only required for a few months. The results can be greatly rewarding to both mother and child.

Infertility

The only area of mainstream medicine where natural progesterone is routinely used is the area of assisted fertility. Natural progesterone injections, high dose natural progesterone pessaries, progesterone gel and micronized progesterone ovules are used to prime the uterus for implantation of a fertilized egg. This use is limited and highly specialized, but does not cover all facets of infertility. Many women have little trouble falling pregnant, however, the failure to carry the pregnancy beyond week six to ten is an all too common experience for many couples.

Once implantation of a fertilized egg takes place in the uterine wall it starts a cascade of hormonal triggers. One of the most important of these is to increase progesterone production from the corpus luteum. The corpus luteum (a yellow mass on the surface of the ovary) formed when the follicle that released the egg metamorphosed. Its role is to secrete progesterone. Progesterone is the vital hormone for propagating pregnancy. The corpus luteum is required to produce sufficient progesterone to maintain the integrity of the uterine lining until the placenta takes over the progesterone production at around week 10. The placenta takes over to meet the increased progesterone demands of the pregnancy.

The most vulnerable time for miscarriage in women who are low progesterone producers during pregnancy is week six to week ten. If the corpus luteum cannot maintain production of sufficient levels of natural progesterone the uterine lining breaks down and sheds, resulting in the miscarriage. It is women with a history of week six to ten miscarriage whom benefit most from supplementing their natural progesterone production with natural progesterone cream.

Often women will use the natural progesterone cream until full term.

Treatment is usually dependent upon how advanced the pregnancy is in relation to commencing progesterone supplementation. For example, if spotting occurs at week six or seven, a high dose of 100-200mg of progesterone cream twice or three times daily is applied. Ideally, a low dose natural progesterone supplementation can be commenced in the months and weeks preceding conception (days 12-26 of the cycle) until the pregnancy is confirmed. After this, maintenance of a low dose, daily natural progesterone supplement is recommended to support corpus luteal production.

Similarly, often for reasons unknown, the mature placenta can under-produce progesterone. The addition of natural progesterone will maintain the integrity of the uterine lining and assist the mother in carrying to full term. It is a treatment option that can do no harm and usually brings much joy.

Hormone-induced Headaches and Migraines

It is common for many women to experience headaches or migraines (in the more severe cases) in the days leading up to their periods. The duration and severity of the headache is nearly always directly related to estrogen dominance and insufficient progesterone production. Similarly, many women cannot tolerate the Pill or hormone replacement therapy (HRT) for the same reason. Adding estrogens into a progesterone-deficient woman increases the degree of estrogen dominance and often results in side effects such as hormone-induced headaches and migraines. Additionally, body aches and pains are usually exacerbated.

The use of pain killers, muscle relaxants and antidepressants do not address the underlying cause of hormone-induced headache and migraine.

The use of ProFeme® natural progesterone cream (Lawley Pharmaceuticals, Australia) from day 12- 26 of the cycle provides the counterbalance to estrogen dominance. It reduces the frequency and severity of cyclical headaches and migraines.

Vaginal Dryness

Vaginal dryness is a symptom which many women find uncomfortable and physically distressing. Fortunately, it is one problem that can easily be helped. A deficiency of estrogen will cause the lining of the vaginal walls to thin, become drier and less elastic (atrophic).

Sexual intercourse is often painful which means most women are less than enthusiastic about sex at this time. Locally acting estrogen creams and vaginal tablets are available. They are not absorbed into the system. The use of progesterone creams externally may help with vaginal dryness by making the estrogen receptors in the wall of the vagina more responsive to naturally produced estrogen.

Breast Cancer

The risk of breast cancer is one of the greatest concerns facing women when they reach menopause and are offered hormone replacement therapy. The issue of breast cancer and estrogens has been highly publicized in the media in recent years. Balancing the risks versus the benefits of using estrogen to manage menopausal symptoms can be difficult to understand given the emotive and often uninformed comment in the media and on the internet. There is probably no single cause of breast cancer. It is most likely a number of triggers - genetic, familial, environmental and even psychological that when combined stimulate the cancers to become active. Dr John Lee, the pioneer of natural progesterone cream for managing menopausal symptoms, wrote a book called, "What Your Doctor May Not Have Told You About Breast Cancer". This work clearly and concisely outlines the vital role progesterone has in the breast and in prevention of breast cancer. It is highly recommended reading.

One of the most controversial breast cancer and natural hormone medical studies ever conducted provides an insight into the positive effect natural progesterone has on cancerous breast tissue. In 1995, a joint French-Taiwanese medical team (Chang et al.) took 40 women with



breast cancer who were scheduled for mastectomy and divided them into four groups. Each group was assigned to a treatment of either estrogen only (E), estrogen and natural progesterone (E+P), natural progesterone (P) only or placebo (PL). The hormones were administered via a gel applied once daily directly to the breasts for ten days prior to surgery. After surgery, the cancerous breast tissue was assayed and the rate of cell division (mitosis) was examined. In breast cancer, as in most cancers, the rate of mitosis of the cancerous cells is more rapid than for non-cancerous cells, hence the reason why cancers take over healthy cells. When the researchers examined the various cell groups treated with the hormones, the results were astonishing. As was expected, the estrogen only group's mitotic cell division rate doubled compared to the placebo (untreated) group. The stimulatory effect of estrogen on cancerous breast tissue is well known. The researchers' excitement stemmed from the results of the estrogen plus natural progesterone and the natural progesterone only groups. The E+P group's mitotic rate was the same as the placebo group. This indicated natural progesterone had an inhibitory effect upon the estrogen's stimulation of the cancerous cells. When the progesterone only (P) group was examined, the rate of cell division was 85% less than the placebo group - natural progesterone was inhibiting the spread of the cancer. Natural progesterone was potentially a potent treatment for breast cancer. This study had its critics. They said the numbers studied were too small to

be significant and the progesterone blood levels of the P and E+P groups did not rise. Therefore, it was considered the progesterone hadn't been absorbed. When the actual tissue concentrations of the cancerous cells were examined, the progesterone was found in very high concentrations in both progesterone groups and absent in the E and PL groups. The progesterone had been absorbed directly into the cells and not circulated in the blood. It was acting directly inside the cancerous cells and the mitotic rates proved it.

Larger scale clinical studies have never been conducted to confirm these findings from 29 years ago. With the modern day rigors and political correctness of Ethics and Scientific Committees, the massive funds required to undertake clinical trials and the complex insurance obligations to undertake such trials, it is unlikely it will be repeated on a larger scale. The pharmaceutical industry's charter is to discover the next blockbuster patentable drug. Natural progesterone does not meet this criteria. The Chang results are compelling and natural progesterone cream is available. With time, progesterone may prove to be the missing link in the quest to prevent and treat breast cancer. The challenge is there for mainstream medical researchers and governments to take up.

Endometriosis

Endometriosis is a condition whereby tissue normally located on the surface of the uterine wall (endometrium) migrates into areas such as the muscle tissue of the uterus, the Fallopian tubes, the surface of the ovaries and even into the pelvic cavity. This tissue is responsive to the surges of estrogen encountered during the menstrual cycle. The tissue will swell during the month and bleed at the same time as menses. Unlike endometrial tissue (the tissue lining of the uterus) which sheds into the uterine cavity, the endometriosis bleeds into the intercellular spaces and has nowhere to go. The condition is painful, often debilitating and may greatly hinder fertility.

Treatment varies from analgesics (pain killers) to high-dose synthetic

progestins, to surgical procedures including hysterectomy.

Often pregnancy, if possible, is suggested as the best treatment. During pregnancy, when progesterone levels are high and estrogen levels relatively low, endometriosis virtually disappears. The very high level of progesterone produced by the placenta during pregnancy suppresses and overcomes the endometrial tissue. Occasionally with the return of menses post-pregnancy, the endometriosis will return.

Endometriosis has various degrees of severity and current treatment is aimed at symptom management. Unfortunately, natural progesterone is rarely offered as an option. Endometriosis is a condition at the extreme end of the scale of estrogen dominance. The underlying cause is progesterone deficiency. Treatment with high dose progesterone cream, even in severe cases, usually achieves improvements in the condition. In milder cases, often there is full resolution of symptoms with pain-free periods. Depending upon the severity of the endometriosis the treatment may take three to six months to achieve full benefit. For many women yet to start a family this is a better option than endometrial ablation, hysterectomy or long-term hormonal suppression.

Natural progesterone cream offers a viable alternative to current mainstream endometriosis treatments because it safely tempers the stimulating effects of estrogen.



Polycystic Ovarian Syndrome (PCOS)

The process of ovulation involves the ovary responding to chemical messengers sent from the brain. The brain controls the chemical signals sent to the ovaries based upon chemical signals it receives back in response to its signals. It's called a feedback mechanism. At birth every female has around 400,000 immature eggs in follicles contained within the ovaries. At puberty the reproductive organs, under the influence of estrogens, mature. A key part in the process of ovulation is when the brain releases the hormones follicle stimulating hormone (FSH) and luteinizing hormone (LH).

FSH stimulates a number of immature eggs to mature and rise to the surface of the ovary. Usually, one follicle releases a mature egg into the Fallopian tubes - this release is called ovulation. The unused semi - mature follicles are broken down and reabsorbed by the body. The follicle that released the egg then undergoes a spectacular metamorphosis. Its entire structure changes and it forms what is called the corpus luteum. Visually, the corpus luteum appears as a yellow mass on the surface of the ovary. It plays the vital role of being the production site for progesterone. The brain detects when the progesterone concentration in the blood increases. In turn, the brain shuts off the production of FSH. This is because it now knows ovulation has successfully taken place. Without the production of progesterone the brain will think ovulation has failed to take place. As a result, it will keep producing FSH and LH to stimulate ovulation. Progesterone is the key!

Women with PCOS fail to ovulate and have very few periods in a year. The follicles mature and rise to the surface of the ovary, but for reasons unknown they fail to release. As a result, the corpus luteum doesn't form and no progesterone is produced. The brain doesn't detect any progesterone rise in the blood and therefore releases more FSH to stimulate more follicles. The surface of the ovary looks lumpy and bumpy with many semi-matured follicles just below the surface all having failed to ovulate. Usually they are arranged in a pearl-necklace

formation. Because of this disruption to the normal hormonal cycle, PCOS sufferers develop higher levels of the hormone testosterone due to increased luteinizing hormone being released from the pituitary gland in the brain. With time, this has the effect on the PCOS sufferer of weight gain, acne and oily skin, and increased facial and body hair. Associated with these physical changes, the body becomes resistant to the effects of insulin and as a result the normal process of sugar metabolism is disrupted. Sugar is converted to fat and the PCOS sufferer usually has significant weight problems. PCOS usually affects younger women and is often undetected for many months and even years. Often symptoms are associated with the physical maturation of the body and expected to settle down with time.

There are numerous synthetic hormonal and non-hormonal options to treat PCOS. Most of these involve the management of symptoms rather than addressing a significant underlying cause – progesterone deficiency.

The Progesterone Deficiency Assessment Questionnaire

Menopause is defined as a woman's last menstrual period. The average age of menopause is 51.

A woman is considered post-menopausal when she has not had a period for 12 consecutive months.

Each woman's transition into menopause is different. Some women have mild and transient menopausal symptoms. Other women find the quality of their lives significantly affected by changes in mood, memory, productivity and uncomfortable physical symptoms. Often the months and years preceding menopause, called peri-menopause, can be severely stressful due to symptoms associated with declining and fluctuating progesterone activity. Quantifying the severity of symptoms can often be difficult because symptoms may vary from day-to-day or week-to-week. What is usually consistent with most women is they

steadily get worse with time. This often leads women to seek medical intervention.

The Progesterone Deficiency Assessment Questionnaire allows for a baseline assessment of symptoms to be made. It provides a valuable tool for the monitoring of whatever method of peri- and menopausal symptoms management a woman chooses to undertake.

The Progesterone Deficiency Assessment Questionnaire can be taken online at www.hormonesolutions.com/fpd

The Progesterone Deficiency Assessment Questionnaire is free.

Symptoms	None	Mild	Moderate	Severe
Water Retention/bloating/weight gain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Increased facial hair	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Breast tenderness/swelling	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Pain: Headache/migraine/low back/muscle ache/joint ache	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Vaginal dryness/pain/itching	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

What Are The Pros And Cons Of Natural Progesterone Treatment Versus Synthetic Progestins?

Naturally occurring hormones (progesterone, testosterone and estradiol) when incorporated into a cream are absorbed through the skin (transdermally), so they avoid first pass metabolism by the liver. First pass metabolism is a phenomenon where ingested drugs are absorbed through the stomach and intestine, travel to the liver, and are broken down to the extent that only a small fraction of the active drug circulates to the rest of the body. This first pass through the liver greatly reduces the availability of the hormones to cells by breaking them down into less active forms. Synthetic forms of progesterone are called progestins. Progestins (such as medroxyprogesterone acetate (MPA), norethisterone, levonorgestrel, drospirinone and desogestrel) are rapidly metabolised by the liver due to the first pass effect, so the

amount of hormone received is significantly reduced. All progestins have side effects not usually associated with natural progesterone. For example, medroxyprogesterone acetate has a very narrow spectrum of action on the uterus and unlike progesterone has significant side effects. It is sold as Provera® as well as under many generic brand names. It is commonly used to treat heavy menstrual bleeding and in hormone replacement therapy.

Medroxyprogesterone acetate (MPA) may cause birth defects if taken during pregnancy. Natural progesterone is the essential hormone of pregnancy. MPA passes into breast milk and damages the infant, so it is not suitable as a treatment for post-natal depression. MPA increases the risk of blood clots, especially in smokers, can cause depression or induce suicidal feelings. It predisposes women to breast, ovarian, and uterine cancer. If medroxyprogesterone acetate is used long-term, it increases the risk of stroke and heart attack. Published side effects of synthetic medroxyprogesterone acetate include weight gain, itchy skin rash, acne, hair loss, insomnia, bloating, menstrual irregularities, vaginal discharge and tender breasts.

Progesterone receptors in the body are extremely fussy as to what “key” switches them on. Progestins such as MPA do not interact with the progesterone receptor in the same way natural progesterone does. Therefore, the estrogen-dominant symptoms do not respond to a progestin in the same way as they do to natural progesterone. In summary: progestins and natural progesterone are worlds apart in their effect and can never be compared for overall effect in treating estrogen dominance.



What is The Role of Progesterone in Humans?

Progesterone is the hormone that regulates menstruation, supports pregnancy, tempers the highly stimulatory effects of estrogen and helps an embryo develop by providing a source of corticosteroids. Natural progesterone is a steroid hormone derived from cholesterol and is vital as a precursor hormone in the body's production of corticosteroids and glucocorticoids – steroids that help us deal with stress and physical cellular/tissue repair.

Progesterone is normally produced by the corpus luteum in the ovaries and in the brains of humans and animals. At about 8 to 10 weeks of pregnancy, the placenta in pregnant females takes over progesterone production from the ovaries. Progesterone is the pivotal hormone of pregnancy. Women in their childbearing years experience cyclical progesterone surges. In the beginning (follicular phase) of a menstrual cycle, women have low progesterone levels equivalent to that in men, children, and post- menopausal women (less than 2 ng/ml of blood). The small amount of progesterone present in males does not have a feminizing effect on them.

Progesterone calms mood in both sexes. When a woman releases an egg for fertilization (ovulation), her progesterone level spikes (greater than 5 ng/ml of blood). If the egg (ovum) is fertilized, the corpus luteum (yellow body) in the ovary secretes progesterone to



maintain the pregnancy until the placenta is large enough to take over production. Progesterone levels increase to 400 ng/ ml of blood, and taper off during the last month of pregnancy to 200 ng/ml. After birth occurs and milk production (lactation) begins, women experience “baby blues” because the progesterone levels decrease abruptly.

Progesterone is a neurosteroid in the brain that affects functioning of the nerve synapses and the protective myelin sheath of nerves. Researchers are investigating the effects of progesterone on memory, cognition, and multiple sclerosis. Animal studies suggest progesterone may protect females from brain injury.

Progesterone reduces spasms in smooth muscles. It is an anti-inflammatory and decreases immune response. Progesterone adjusts the body's use of zinc, copper, fat, estrogen, collagen, and blood clotting factors. It is a hormone that influences the function of the uterus, gall bladder, thyroid, bones, teeth, skin, ligaments, tendons, and joints.

Are There Side Effects Associated With Using Natural Progesterone?

ProFeme® natural progesterone cream has very low toxicity. The most common problems associated with progesterone treatments are they can cause symptoms similar to the feeling of pregnancy:

- Tender breasts
- Fatigue
- Mood swings
- Constipation or diarrhea
- Headache
- Muscle or joint pain
- Occasional breakthrough bleeding (spotting)
- Fluid retention
- Dizziness

If these occur, a simple adjustment of dose usually resolves the problem. If they are to occur, side effects are usually experienced at the onset of treatment and are considered a positive sign. They usually resolve themselves fully within 10 days of a dose reduction and often sooner.

What About Homeopathic and Herbal Treatments?

Homeopathy is a complementary therapy. Homeopaths claim that like cures like. Essentially, homeopaths believe if a substance causes a disease, then you can cure it by taking a very minute, diluted amount of the same substance.

Homeopathic treatments contain NO testosterone, nor have they been demonstrated to cause any change in testosterone hormone levels. Be very careful when ordering products online that claim to contain testosterone, because usually they contain homeopathic forms of testosterone which are ineffective.

Additionally, the herbs tribulus, horny goat weed, tongkat ali extract (*Eurycoma longifolia*) and mucuna pruriens extract have not been shown in scientific testing to increase blood testosterone levels despite extravagant marketing claims.

Natural Progesterone Treatments

Sadly, medical researchers have failed for decades to study in detail the multitude of beneficial effects of natural progesterone. Natural progesterone cream or micronized progesterone capsules have stood the test of time as an effective, safe and reliable mode of administration for the management of progesterone deficiency conditions.

Other forms of natural progesterone such as lotions, gels, sprays and troches have not proved to be as effective as natural progesterone cream for the management of symptoms. If one Googles “natural progesterone cream” there are dozens of products claiming to be the “best” or “authentic” natural progesterone creams. Just how does a woman contemplating using a natural progesterone cream determine which is the product most suited to her requirements?

Understanding the basics of the various manufacturing processes is a good start in determining what constitutes a quality natural progesterone cream. Standards of manufacture and clinical efficacy

are the two yardsticks by which to assess the most superior natural progesterone creams available.

There are three standards of natural progesterone cream production.

- Pharmaceutical grade
- Cosmetic grade
- Compounded products

Pharmaceutical Grade - manufacture operates to international standards of Good Manufacturing Practice (GMP). GMP standards demand all production processes are standardized and controlled from the raw material procurement through to the expiry date of the finished product. The rigid government controls on the manufacturing facility, manufacturing equipment and processes, final product packaging, stability, efficacy and potency, product documentation and clinical trials for efficacy guarantee the quality of the final product. Therapeutic claims are required to be substantiated.



Cosmetic Grade - manufacture does not have the same rigid government rules and regulations associated with pharmaceutical grade manufacture. There are not equal obligations upon cosmetic manufacturers to deliver the same scientifically exact concentration of finished product as demanded of pharmaceutical grade products. Stability requirements of cosmetic grade products are not as onerous

as for pharmaceutical grade items. Therapeutic claims of cosmetic items are limited, if claims are not substantiated.

Compounded Products - are items made by pharmacists in the confines of a pharmacy. Compounded products are made by hand on an individual patient basis. Compounded products do not undergo any form of production control, concentration, impurity, stability or efficacy testing.

The legal status in relation to access to natural progesterone creams depends upon each particular country's scheduling requirements. In the USA, natural progesterone creams are available over-the-counter provided manufacturers make no therapeutic claims for the products. Disclosure on the labels of the concentration of progesterone within the finished product can be "ambiguous". In the UK and Australia, natural progesterone cream is classified as a prescription only medicine.

There is only one pharmaceutical grade natural progesterone cream available worldwide, ProFeme® 3.2% or 10% progesterone cream by Lawley Pharmaceuticals, Australia.



Natural Progesterone for Women – Quick Q & A

Q. Is the progesterone in ProFeme® “natural” progesterone?

A. Yes. ProFeme® is guaranteed 100% to contain “natural” progesterone. Natural progesterone was the term coined by US doctor John Lee M.D. to differentiate between the chemical structure of progesterone produced by the ovaries (“natural”) and the chemical structures of the synthetically produced progestins. Progestins are often confused with progesterone. Their chemical fingerprint is totally different and natural progesterone has a far greater diversity of action than progestins.

Q. Does the wild yam contain natural progesterone?

A. No - definitely not. The wild yam contains a steroid substrate called diosgenin that is similar in its chemical structure to progesterone. Diosgenin, however, does not act like progesterone within the body. The human body is unable to convert diosgenin into progesterone - a point often misrepresented by marketers of wild yam products.

Q. Where does “natural” progesterone come from?

A. Wild yam and soya are the two crops which contain steroid substrate (diosgenin and stigmasterol - plant hormones) similar in their chemical structure to progesterone. Because these two crops are grown in commercial quantities, large quantities of raw substrate material can be extracted. Diosgenin and stigmasterol are converted in a laboratory to make “natural” progesterone. This is the same chemical structure as produced by the ovaries and is identical in every way.

Q. Is the progesterone in the Lawley ProFeme® progesterone creams made from genetically modified soya?

A. No - Lawley Pharmaceuticals in Australia, the manufacturers of the cream, has documentation from the raw material manufacturers stating the progesterone is not produced from genetically engineered soya crops.

- Q.** How long before the ProFeme® progesterone cream helps my PMS or menopausal symptoms?
- A.** Usually it takes between four and eight weeks for the cream to reverse symptoms. Many people want an overnight cure to their menopausal problems or PMS symptoms. It must be remembered the underlying hormone imbalance that led to the point where symptoms warranted treatment usually developed over many months, if not years. They cannot be reversed overnight. Most people find symptoms improve steadily with each month of use. After about 12 months use maximum effect is achieved.

Suggested Reading

- Natural Progesterone - The world's best kept secret. By Jenny Birdsey
- Natural Progesterone. More secrets revealed. By Jenny Birdsey
- Once A Month – Understanding and Treating PMS. By Katharina Dalton, M.D. Hunter House Publishers
- Woman to Woman : managing your hormones safely and naturally. By Kim Balson N.D.
- What Your Doctor May Not Tell You About Menopause. By John Lee, M.D. with Virginia Hopkins. Warner Books
- Passage to Power. By Leslie Kenton. Elbury Press. Random House

Links to Natural Progesterone Information

To learn more about progesterone for women, testosterone for men and testosterone for women, log onto www.hormonesolutions.com or call Lawley Pharmaceuticals on 1800-961-7813.

About Lawley Pharmaceuticals

Lawley Pharmaceuticals is a privately owned pharmaceutical company which focuses on the transdermal administration of the naturally occurring hormones progesterone, testosterone and estradiol. Founded in 1995 by pharmacist Michael Buckley, Lawley Pharmaceuticals has grown to become a world leader in research and development of transdermal hormone preparations.

AndroFeme® 1% testosterone cream for women



AndroForte® 2% and 5% testosterone creams for men



ProFeme® 3.2% and 10% progesterone creams for women



Our Mission Statement

Lawley Pharmaceuticals (www.hormonesolutions.com) strives to provide the optimal delivery systems for the administration of the naturally occurring human hormones (testosterone, progesterone, estradiol and estriol) to counter endocrine deficiency states.

Our philosophy is to use a natural hormone in preference to a synthetic hormone when a viable clinical option and to advance areas of clinical research using natural hormones.

Our goal is to establish, through evidence-based medical research, naturally occurring hormones as cornerstone treatments for diseases such as breast cancer, infertility, first-term miscarriage, male hypogonadism, post-partum depression and endometriosis.

Lawley Pharmaceuticals has established strong links with centers of medical research excellence around the world and continues to push the boundaries of medical research.

Completed Clinical Studies

1. Effect of sequential transdermal progesterone cream on endometrium, bleeding pattern, and plasma progesterone and salivary progesterone levels in postmenopausal women. Wren BG et al. *Climacteric* 2000 3:155–160.
2. Distribution and metabolism of topically applied progesterone in a rat model. Waddell B and O’Leary PJ. *J Ster Biochem & Mol Biol.* 80 (2002) 449–455.
3. Plasma and saliva concentrations of progesterone in pre- and postmenopausal women after topical application of progesterone cream. O’Leary PJ et al. Presented at the Annual Congress of the Australian Menopause Society held in Perth, Australia in October 1997.
4. Long-term pharmacokinetics and clinical efficacy of ANDROMEN® FORTE 5% cream for androgen replacement in hypogonadal men. Handelsman DJ et al. ANZAC Research Institute, Department of Andrology, Concord Hospital, Sydney, 2004.
5. Transdermal testosterone therapy improves well-being, mood, and sexual function in premenopausal women. Goldstat R et al. *Menopause* 2003; 10 (5): 390-398.
6. The pharmacokinetics pilot study of ANDROFEME® 1% testosterone cream following two-week, once-daily application in testosterone-deficient women. Eden JA et al. Presented at the 4th Annual Congress of the Australasian Menopause Society held in Adelaide 5-7th November 2000.
7. A double-blind, randomized, placebo-controlled trial of the effect of testosterone cream on the sexual motivation of menopausal hysterectomized women with hypoactive sexual desire disorder. El- Hage et al *Climacteric* 2007; 10: 335–343.
8. Pharmacokinetics of ANDROMEN® FORTE 5% Cream: A Dose Finding Study. Kelleher S et al. ANZAC Research Institute, Department of Andrology, Concord Hospital, Sydney, 2002.
9. The Pharmacokinetics of AndroForte® Compared With AndroGel® (Testogel®) in Androgen Deficient Men. Wittert G et al. Adelaide Awaiting publication.

Copyright Information

© Lawley Pharmaceuticals 2014

This publication is copyright. Other than for the purposes of and subject to the Copyright Act, no part of it may in any form or by any means (electronic, mechanical, microcopying, photocopying, recording or otherwise) be reproduced, stored in a retrieval system or transmitted without prior written permission.

All inquiries should be addressed to Lawley Pharmaceuticals.

This brochure is presented by

Lawley Pharmaceuticals

2/15A Harrogate St, West Leederville 6007, WA Australia

T. USA and Canada Toll free phone: 1-800-961-7813

F. Toll free fax: 1-800-961-7650

E. info@hormonesolutions.com

W. www.hormonesolutions.com

LAWLEY

Hormone Solutions