

Understanding endometrial hyperplasia



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Hormone Solutions

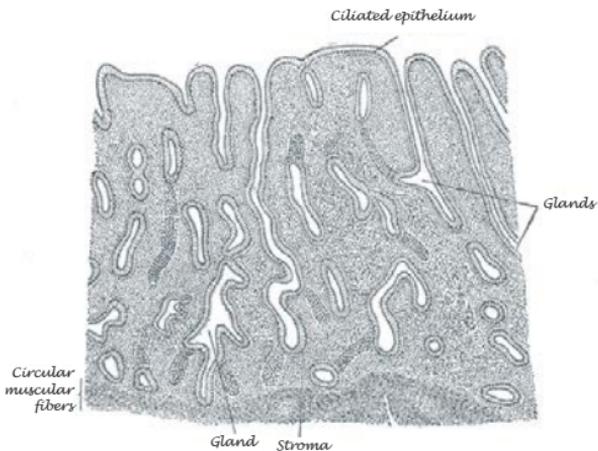
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What is endometrial hyperplasia?

Endometrium is the lining of the womb (uterus), which is normally shed every month during the childbearing years, unless the woman conceives. **Endometrial hyperplasia** is overgrowth of the lining of the womb, beyond the normal 5 millimeters in thickness. It is also called endometrial hypertrophy. Hyperplasia can occur throughout the entire uterine lining, or may only affect an isolated area. *Endometrial hyperplasia is not cancer*, but it can cause cellular changes that predispose an affected woman to developing cancer later. Most endometrial hyperplasia develops from a hormonal imbalance, where there is a [dominance of estrogen](#) and a deficiency of progesterone.

Normal structure and function of endometrium



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Normal endometrium is one layer of epithelium, the tissue that lines organs, resting on a stroma, a mat of connective, supportive tissue. A fertile woman has a functional layer of endometrium next to her empty uterine cavity, and a basal layer riding over the muscle of her uterus, the myometrium (not shown on above diagram). *Only the functional layer is shed during menstruation.* If the woman does not conceive, myometrium contracts to expel the endometrium through the vagina as part of the normal menstrual flow. Myometrium also expels the fetus during childbirth.

Normal epithelium is columnar, meaning its length is four times its width. Glands run from the top of the endometrium down into the stroma. Spiral arteries feed the endometrium with blood.

From Day 1 to Day 4 of a normal menstrual cycle, when you are bleeding, the endometrium is thin because the functional layer (epithelium) is absent. During the estrogen phase (first half of a normal cycle, from Day 4 to Day 14), the lining of your uterus proliferates or grows. Proliferative endometrium has tubular glands and columnar cells. *Proliferative endometrium does not shed, but continues to build up unless the estrogen is opposed by progesterone.* At mid-cycle, around Day 14, your ovary releases an egg for fertilization (ovulation) and produces progesterone. **Progesterone is only produced once ovulation occurs.** Progesterone makes the lining of your uterus hospitable for an embryo. During the progesterone (luteal) phase (second of a normal cycle, from Day 15 to Day 28), your endometrium secretes and is thick. Secretory endometrium has winding (tortuous) glands with vacuoles or bubbles. If conception does not take place, *only secretory endometrium sheds during menstruation.*

Endometrium is the blood-rich tissue that nourishes the fertilized egg when it first implants in the uterus. If the woman conceives, the blood vessels and glands of the endometrium (decidua) fuse to become the **placenta**, which sustains her pregnancy. If a woman does not consistently release an egg at mid-cycle ([anovulation](#)) then there is a sustained absence of progesterone. The lining of her

uterus may become abnormally thickened due to the dominance of estrogen and her periods will be very heavy ([menorrhagia](#)) and often painful ([dysmenorrhea](#)). An infertile woman may have no periods (amenorrhea) or infrequent periods (oligomenorrhea).

A menopausal woman who is taking estrogen replacement therapy and has not had a hysterectomy requires progesterone supplements to prevent the lining of her uterus from thickening and bleeding from resuming. Estrogen replacement therapy (ERT) alone can make your endometrium dangerously thick (hyperplastic) and prone to cancer.

Types of endometrial hyperplasia.

There are four types of endometrial hyperplasia: Simple, complex, simple atypical, and complex atypical. Simple and complex refer to architecture (overcrowded and intricate glands). If you develop endometrial hyperplasia, remember that 90% of simple and complex cases resolve spontaneously or with medical management. Atypia refers to changes in cell cytology and behaviour that is precancerous or cancerous. Patients with atypia are more likely to develop cancer, and are candidates for hysterectomy.

Simple

Simple hyperplasia is also called **Swiss cheese endometrium**, because the glands resemble the irregular holes in cheese as they dilate and form cysts separated by abundant stroma. Simple hyperplasia causes heavy bleeding but very rarely develops into cancer (less than 2%). The glands are not back-to-back. There are no precancerous changes in the cells.

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Complex

Complex hyperplasia is also called **adenomatous hyperplasia**. There is still only one layer of endometrium. The glands are bunched together back-to-back, instead of evenly distributed, and develop tufts. There is very little stroma. A few of the basal cells may have slightly enlarged nuclei, a change that predisposes the woman to developing endometrial cancer later.

Simple atypical

There is abundant stroma. The glands are enlarged, especially their nuclei. The cells have different forms as they age (pleomorphism). The endometrial cells multiply too quickly, which is a feature of cancer. However, the endometrial cells have not yet penetrated into connective tissue, as true cancer would.

Complex atypical

The glands stratify into layers and crowd together back-to-back. The epithelium forms tufts. The cells develop very dark, large nuclei. The cells can go through many forms as they age (pleomorphism).

What are my odds of developing cancer?

Only 1% of simple hyperplasia cases develop into cancer. Only 3% of complex hyperplasia cases develop into cancer. Only 8% to 10% of simple atypical hyperplasia cases develop into cancer. Unfortunately, 30% of complex atypical hyperplasia cases develop into cancer. Ninety percent of uterine cancers start in the endometrial lining. White women are more prone to endometrial cancer. Less than 10% of uterine cancers start in the muscle layer (myometrium), which is called uterine sarcoma. Black women are more prone to uterine sarcoma. Three percent of women will develop endometrial cancer. Seventy-five percent of women who develop uterine cancer are

postmenopausal, usually around 60 years of age. Women under 40 who develop hyperplasia tend to have [polycystic ovarian syndrome \(PCOS\)](#), or they are infertile because they do not ovulate, or they are chronically obese.

One-third of women with hyperplasia develop endometrial carcinoma

Why is hyperplasia dangerous

Initially, endometrial hyperplasia causes very heavy menstruation, which can lead to iron deficiency anemia (IDA). An anemic woman feels tired, depressed, irritable and withdrawn because her blood cells cannot carry enough oxygen to supply the needs of her body. As the anemia worsens, the affected woman will probably perform badly at study or work because of cognitive problems. Severe anemia leads to chest and abdominal pain, fainting, and breathing difficulties.

If the hyperplasia overgrows to the extent that it penetrates the muscle layer of the uterus (adenomyosis), then the endometrium is precancerous and menstruation becomes painful.

Left untreated, the constant irritation of endometrial hyperplasia can cause the cells of the uterus to change. If your endometrium measures less than 5 mm, there is a 98% chance that you do *not* have cancer. An endometrium thicker than 5 mm has a 7.3% chance of harboring cancer. Menopausal women with cellular changes in their endometria are more likely to develop cancer than women of childbearing age.

POLYSYSTIC OVARIAN SYNDROME (PCOS)

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What causes hyperplasia?

Endometrial hyperplasia usually results when the lining of the uterus is exposed to estrogen in the absence of sufficient progesterone. The cause can be:

- [Progesterone deficiency](#)
- [Polycystic ovary syndrome \(PCOS\)](#)
- [Perimenopause](#)
- Obesity with diabetes
- Using tamoxifen to suppress breast cancer
- Using estrogen supplements alone, without progesterone, to suppress the effects of menopause
- Ovarian tumor
- Inherited cancer of the bowel (hereditary non-polyposis colorectal carcinoma)

Who is at risk for hyperplasia?

You are more likely to develop endometrial hyperplasia if you:

- Started menstruating before age 12
- Have never given birth
- Are white (caucasian)
- Take tamoxifen (Nolvadex[®]) to prevent breast cancer
- Have a breast cancer tumor that secretes estrogen hormone
- Have ovarian cancer
- Take estrogen replacement therapy alone, without progesterone, after menopause
- Experience menopause after age 52
- Are obese
- Have diabetes
- Have high blood pressure (hypertension)

- Have gall bladder disease
- Have a family history of uterine cancer
- Received pelvic radiation
- Are older than 50

Women who take combined birth control pills are less likely to develop endometrial hyperplasia.

What are the signs and symptoms of hyperplasia?

Endometrial hyperplasia can begin as:

1. **Vaginal discharge**, especially if it has an odor
2. **Amenorrhea**, lack of a menstrual period for more than 90 days, and you are not entering menopause
3. **Menorrhagia**, excessive bleeding greater than 80 milliliters (more than 16 soaked sanitary pads or 1/3 cup of blood) during the regularly expected menstrual period OR
4. **Metrorrhagia**, irregular uterine bleeding between expected menstrual periods OR
5. **Menometrorrhagia**, heavy *and* irregular uterine bleeding during the expected menstrual period and also at irregular, unexpected intervals OR

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6. **Polymenorrhea**, bleeding too frequently, less than every 21 days OR
7. **Post menopausal bleeding (PMB)**, when a woman over 40 who has not bled for at least 18 months resumes bleeding, AND her doctor has verified her menopause through blood tests for hormone levels
8. **Difficult urination**
9. **Dyspareunia**, pain during sexual intercourse

Do not panic if you have any of these symptoms, however medical investigation is required.

Well advanced uterine cancer causes pelvic pain, loss of appetite (anorexia), weight loss, and bowel and bladder changes.

What is a normal cycle?

Length

Most women have one menstrual cycle every 22 to 35 days. Day 1 is the first day of menstrual bleeding. Day 1 should be the day when the heaviest bleeding occurs. Bleeding should last only 4 to 6 days.

A few women have a regular cycle of 18 to 40 days, and if that is consistent, fairly painless, and not excessively heavy or light, then it is considered a normal variation.

Eighty percent of bleeds last three to six days, which indicates an ovulatory cycle, during which an egg was released for fertilization. Bleeds lasting longer than eight days indicate dysfunctional ovaries. The problem could be **anovulation**, meaning no egg was released by the ovary for fertilization, or inadequate hormones in the second half of the cycle (luteal phase). The hormone **progesterone** is supposed to be the dominant hormone in the second half menstrual cycle. **A deficiency of progesterone is crucial to the origins of developing endometrial hyperplasia.**

Quantity

Normal blood loss is 10 to 35 ml, or 2 to 7 soaked sanitary pads per cycle. The absolute maximum blood loss during a heavy cycle should be 45 to 60 ml. If it exceeds this amount, the woman is at risk of developing iron deficiency anemia and will have a difficult pregnancy.

A regular menstrual pad or tampon holds around 5 milliliters (mL) of blood. To calculate the approximate amount of blood you have lost if you wear regular pads or tampons, multiply the number you used by the number of days you have been bleeding. For example:

10 regular pads X 5 days = 50 mL of blood lost
([A heavy period](#))

An overnight pad or super tampon holds around 10 mL of blood. To calculate the approximate amount of blood you have lost if you wear extra-absorbent pads or tampons, multiply the number you used by the number of days you have been bleeding. For example:

20 extra-absorbent pads X 10 days = 200 mL
([Menorrhagia](#))

In the first example, you do not usually require treatment for a heavy period. In the second example, you require treatment for menorrhagia

Contact a doctor immediately if you soak a pad every hour for 8 hours. You need to address matters if your period is very heavy for three or more cycles, or if you spot between periods. If you have only proliferative endometrium or a mixture of proliferative and

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MENORRHAGIA www.understandingmenorrhagia.com

secretory, then you will bleed for a very long time, perhaps weeks or even months in a row – this needs treatment for quality of life and to prevent iron deficiency anemia.

The type of birth control used influences blood loss. Women on The Pill lose less blood. Women using IUDs lose more blood.

Appearance

Normal menstrual blood is dark or brownish, not bright red. Normal menstrual blood does not clot easily because it:

- Is high in calcium
- Lacks the clotting factor called prothrombin
- Has very low levels of the clotter fibrinogen

How can I decrease my symptoms?

If heavy bleeding occurs try these easy steps to control bleeding:

1. Bed rest.
2. Drink several salty liquids, like V8, tomato juice, or bouillon soup. Good fluid balance will help keep you from getting dizzy.
3. Take one or two 200 mg tablets of ibuprofen every 4 to 6 hours. Avoid taking aspirin, because it is an anticoagulant and could worsen your bleeding. Ibuprofen will lessen your cramps by decreasing prostaglandins and reduce the blood flow 25% to 30%.
4. Take one 300 mg tablet of ferrous gluconate (or iron alternative) per day to prevent anemia.

Do not take iron supplements regularly without consulting your doctor, because they can cause iron overload. Next cycle, start the ibuprofen 72 or 48 hours before you anticipate bleeding. It will prevent prostaglandins from forming in your uterine muscles, and will reduce your pain.

Losing weight if you are obese helps reduce your symptoms, because fat is a repository of estrogen. Avoid estrogen-mimicking chemical toxins in the environment, such as: Pesticides on produce, phthalates in cosmetics and plastics, and antibiotics and growth hormones in meat and milk. These xenoestrogens reside in your fatty (adipose) tissue.

Avoid cold temperatures. In 1985, Mergler and Vezina found women who worked in cold slaughterhouses were more likely to have [dysmenorrhea](#) (painful periods) and to miss work.

Eat small, protein-rich meals every 3 hours to reduce your symptoms. Energy expenditure increases by 9% to 16% during the luteal phase (second half of the menstrual cycle). Women consume about 500 calories more during the luteal phase than they do in the follicular phase (first half of the cycle), mostly by increasing their carbohydrate intake by 50%. Hormonal changes in the luteal phase alter carbohydrate metabolism, insulin sensitivity, and carbohydrate storage.

What can I expect at my doctor's visit?

Pre-visit

Before you visit your doctor, keep a menstrual calendar of when you bleed and when you feel ovulation. A sample Symptom Tracker is enclosed at the end of this booklet. Note specifically when you feel any symptoms, like dizziness or vomiting. Note down how many pads or tampons you use. Under the "Other" category, list any abnormalities such as nipple discharge, facial or chest hair growth, weight gain or loss (not from dieting), or deepening voice.

Discuss the possibility of changing contraceptives with your sex partner(s). Copper IUDs increase menstrual blood loss by 50% and commonly cause cramping. Progestin IUDs (Mirena®) reduce

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bleeding and can remain inserted for up to five years. Combined oral contraceptive pills (COC) reduce menstrual blood loss 50% and provide pain relief for 70% to 80% of women who have primary [dysmenorrhea](#) (painful menstruation). Your doctor may suggest you change birth control methods at your forthcoming appointment.

History and Physical Exam

The nurse records your vital signs (height, weight, blood pressure and temperature). The nurse and/or doctor will take your pulse twice, first when you have been lying down quietly for 5 minutes, and secondly when you have been standing fairly still for 1 to 3 minutes. The maximum amount your pulse should increase from lying to standing is 20 beats per minute. *If you have bled so much that your blood volume is depleted, your pulse will increase by more than 20.*

Be prepared to answer many personal questions from your doctor about you: Sex history; general health; genetic diseases in your family; previous illnesses; drug use (prescription and recreational street drugs); and stressors. Your doctor will then ask about the length and regularity of your menstrual cycle, and how many pads or tampons you use each cycle.

Pap smear

The Australian government mandates that all women should have a routine Papanicolaou (Pap) smear every two years. New Zealand, Canada, the U.S.A., France and Britain recommend a Pap smear every three years. If you develop any of the signs or symptoms of hyperplasia, do **not** wait until your next scheduled Pap test. Ask your doctor for a thorough examination of your vulva, vagina, and a cervical smear to rule out causes of bleeding in your lower genital tract. The sooner abnormal cells are detected, the better your chances are of a full recovery.

If you have never had a Pap smear before: Remove your clothing from the waist down, and cover yourself with the gown provided.

Recline on the examination couch with your feet in the stirrups. Your doctor shines a bright light on your perineum to see clearly. Your doctor inserts a clean clamp (speculum) into your vagina to hold it open, which feels cold. Your doctor collects a small sample of cells from your cervix by scraping it gently with a Popsicle stick. He or she smears the sample on a glass slide and covers it with a hairspray-like fixative so it will not be washed away when the lab stains it. He or she will swab your vagina with a long-handled Q-tip to check for yeast (*candida albicans*), Chlamydia, trichomoniasis, gonorrhea, and other infections as a routine precaution. The procedure may be uncomfortable but is not painful. Lab results usually take up to a week to be reported.

Blood Tests

Your doctor orders these blood tests for anemia if you menstruate heavily:

TEST		NORMAL ADULT NON-PREGNANT FEMALE VALUE
Complete Blood Count (CBC)	Red Blood Cells	4.2 to 5.4 million/mm ³
	White Blood Cells	5,000 to 10,000/mm ³
	Hemoglobin	12 to 16 g/dl
	Hematocrit	37% to 47%
	Platelets	150,000 to 400,000 mm ³
	MCV	80 to 95 μm ³
	MCH	27 to 31 pg
	MCHC	32% to 36%
	Retics	0.5% to 2% of total RBC
Iron Studies	Serum Iron	60 to 190 μg/dl
	Ferritin	12 to 300 mg/L or 56 ng/ml
	TIBC	250 to 420 μg/dl

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The lab technologist examines your blood smear under a microscope to see if your red blood cells are too pale or too small, indicating your bone marrow is trying to compensate for lack of iron by quickly producing more red blood cells. Your doctor may follow up with an erythrocyte protoporphyrin blood test.

If your doctor suspects you are entering [menopause](#), have [PCOS](#), or another hormonal imbalance, he or she orders these additional tests:

PROFILE	TEST	NORMAL ADULT NON-PREGNANT FEMALE VALUE
Thyroid	T3 T4 TSH	110 to 230 ng/dL 5 to 10 µg/dL 1 to 4 µU/mL
Liver	AST ALT ALP Bilirubin Cholesterol	5 to 40 IU/L 5 to 35 IU/L 30 to 85 ImU/mL 0.1 to 1.0 mg/dL 150 to 250 mg/dL
Kidney	Creatinine BUN	0.7 to 1.5 mg/dL 7 to 20 mg/dL
Adrenals	Cortisol ACTH	2 to 28 µg/dL depending on time of day 15 to 100 pg/mL
Hormones	GH FSH LH HCG Progesterone Estradiol	0 to 8 ng/mL 3 to 20 mIU/mL <7 mIU/mL Negative unless pregnant <2 ng/mL before ovulation >5 ng/mL after ovulation Varies from 25 pg/mL (150pmol/L) on Day 3 to 200 pg/mL (1200pmol/L) at ovulation

PROFILE	TEST	NORMAL ADULT NON-PREGNANT FEMALE VALUE
	Prolactin	< 24 ng/mL
	Testosterone	28 to 80 ng/dL
	Free Testosterone	1.0-2.8 nmol/L
	Free Androgen Index (FAI)	1.3-6.8pg/mL
	SHBG	4.5-23.6 pmol/L
		2-6
		18 to 114 nmol/L

These are guidelines only. Pregnant women, children and men have different normal values. Your laboratory adjusts its normal values for the local population it serves. It may use different units of measure. If the results of your hormone tests are abnormal, your family doctor refers you to an endocrinologist or medical gynecologist.

Transvaginal Ultrasound

The nurse schedules an appointment with Diagnostic Imaging for a transvaginal ultrasound, to measure the thickness of your endometrium and to find any obvious internal causes of bleeding, such as polyps and fibroid tumors.

A transvaginal scan is a painless ultrasound that takes about 30 minutes. Drink eight glasses (32 ounces) of water one hour before you go to the Diagnostic Imaging Lab, and retain your urine until after the scan has been completed. Drinking liquid provides contrast between the uterus and the nearby bladder. You must remove your clothing from the waist down and wear a gown.

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First, the technologist records a pelvic ultrasound. The technologist coats your abdomen with electrolyte gel and moves a transducer across your pelvis to view your ovaries, fallopian tubes, and uterus on a monitor. The technologist is looking for an abnormally shaped uterus, scars, polyps, fibroids and cancer. The technologist may use a Doppler “gun” to determine if any blood vessels are blocked.

The technologist will ask you to empty your bladder for the transvaginal ultrasound. The technologist covers the small probe with a condom, coats it with lubricating gel, and inserts two or three inches of it into your vagina to measure the thickness of your endometrium. An endometrium more than 5 mm is considered too thick, and is the cause of your heavy bleeding ([menorrhagia](#)).

Endometrial Biopsy

An abnormal uterine ultrasound that does not show an obvious polyp or fibroid requires further investigation by microscopic examination. An endometrial biopsy also enables the pathologist to determine if your endometrium is reacting properly to the stimulation of the hormones estrogen and progesterone. It takes 5 to 15 minutes to collect an endometrial biopsy sample. If you are pregnant and wish to carry it to term, inform your doctor, as a biopsy would terminate the pregnancy and should not be performed. If your vaginal swabs showed an infection of any kind, then the biopsy cannot proceed until you are clear of disease. To do so can spread the infection.

Schedule the uterine biopsy for a time when you will not be actively bleeding, so the doctor can reach right down to the uterine wall. A uterine biopsy can be performed in your doctor’s office. No anesthetic is required, but take two ibuprofen capsules (Advil®, Nuprin® or Motrin®) an hour before the procedure to minimize cramping. Wear a sanitary pad afterwards. Do not wear tampons, as they are not sterile and could introduce an infection. Do not douche before or after the biopsy. Schedule the day off work.

Your family doctor or gynecologist has two options for performing the biopsy, either with pipelle or washing, brushing and aspiration:

Pipelle

Your doctor inserts a clean clamp (speculum) into your vagina to hold it open. Your doctor holds your cervix steady with another clamp (tenaculum). A pipelle is a thin, flexible tube your doctor passes through your cervix and into your womb. Your doctor applies gentle suction to vacuum out a small sample of endometrium through the tube, which is then sent to a pathologist for expert microscopic examination. The pipelle method is generally the least painful and time-consuming.

Brushing, Washing and Aspiration

The doctor brushes the endometrium to loosen some cells, and then washes them free with a jet of liquid (irrigation). He or she then applies gentle suction from a Vabra aspiration machine, or similar device, to collect the sample. Brushing, washing and aspiration causes more cramping than a pipelle.

You may sweat profusely, experience a tingling sensation, feel dizzy, nauseated or faint during your biopsy. Tell the doctor and nurse at once if you feel like vomiting or fainting. These responses are a natural vasovagal reaction from fear, pain, and trauma stimulating your nervous system, and will pass when the biopsy is finished. Try to persevere with the test. If an insufficient sample is collected, the pathologist may not be able to reach a conclusive decision, and you will need the test repeated.

Endometrial biopsy is a blind procedure. There is a slight chance you may have prolonged bleeding or infection after a biopsy. If you develop pelvic pain, fever, copious bleeding, foul-smelling vaginal discharge, or if bleeding lasts more than a week, seek medical attention.

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Your biopsy results may be within **normal** limits, meaning the pathologist found no abnormal cells or cancer, and that the cells looked right for the *timing* of the phase when the biopsy was collected during your menstrual cycle.

Abnormal biopsy results indicate that the endometrium may not appear right for the phase in which it was collected during your cycle. If the pathologist found your endometrium is too thick, then it is not cycling properly through proliferation and secretion. Only secretory endometrium can shed. It was probably all proliferative or mixed proliferative and secretory growth. The glands are enlarged and irregular. There may be abnormal cells, called atypia.

Hysteroscopy

If a polyp, fibroid, suspicious growth, or a misshapen uterus is discovered through an ultrasound, your doctor will follow up with a hysteroscopy. A hysteroscopy is an invasive procedure where the doctor looks inside the uterus with a tiny telescope and a thin, flexible “straw” called a hysteroscope. It is usually performed as an out-patient procedure at a hospital or gynecology clinic. Schedule the day off work. Shower the night before your procedure. Do not eat or drink from midnight until your procedure is completed.

In addition to the technologist, a hysteroscopy requires the presence of a radiologist, a doctor specially trained to interpret the images. A doctor is absolutely required because there is a slight chance (0.012%) you could develop complications, such as:

- Adverse reaction to the anesthetic
- Torn cervix
- Leaking of the distention gas or liquid into the bloodstream
- Perforated uterus
- Hemorrhage
- Adhesions
- Infection

You will receive a local anesthetic in your cervix so you will feel no pain. Ask for an epidural or general anesthetic if the procedure makes you very apprehensive. Your cervix may be gently dilated before introducing the “straw”. Gas or liquid is piped through the hysteroscope to widen the uterus and make its interior visible.

If the radiologist discovers a problem, he or she will take a small tissue sample for the pathologist to examine. If there is an obvious mechanical problem causing your heavy bleeding (menorrhagia), like a misplaced IUD, the radiologist will call a gynecologist to consult. The gynecologist may be able to fix the cause on the spot.

How is hyperplasia treated?

Treatment options depend on the type of hyperplasia:

Simple

Simple hyperplasia with no atypical cells in the smear responds very well to progesterone or progestin treatment. You can receive natural progesterone as a topical skin cream (PROFEME®) or a vaginal gel or the alternative is a synthetic progestin tablet or intrauterine device (IUD).

Pure progesterone has fewer side-effects compared with synthetic progestins in the form of an IUD or pills. About 86.5% of patients with simple hyperplasia find it regresses successfully with progesterone or progestin treatment. Progesterone instigates regular and predictable periods. When you stop taking progesterone/progestin each month, your *entire* endometrium will shed at once, and you will not have prolonged bleeding. There will be no dangerous build-up lining your uterus because your period has been hormonally induced and your natural estrogen production is balanced with progesterone. You require a follow-up examination after three months to verify that your hyperplasia has cleared. If your hyperplasia is resistant to the initial treatment doses then your doctor will likely step up the daily dose without a break for six months. If you initially use pure

progesterone ([PROFEME®](#)) and the hyperplasia does not reduce and periods stabilize within 3 months they will usually switch to the stronger synthetic progestin.

Complex

Many doctors recommend Dilatation and Curettage (D&C) as an initial treatment for complex hyperplasia followed by progesterone ([PROFEME®](#))/progestin treatment.

A D&C allows your doctor to remove your built-up endometrium and collect a tissue sample for Pathology at one fell swoop. **However, it is only a temporary solution.** *A D&C does not cure hyperplasia, because the endometrium starts to grow back in the next cycle.*

Alternatively your doctor may offer you triptorelin (Trelstar®, Diphereline®) for 6 months. It is a gonadotrophin-releasing hormone analogue (GnRHa) that regresses complex hyperplasia for 85.7% of patients, but 7.1% have persistent hyperplasia, and another 7.1% progress on to atypical complex hyperplasia (precancer). Side effects can be bothersome.

Simple atypical

Megace® (megestrol acetate) – a strong progestin - for six months is the first line defense for atypia. If unsuccessful, then your doctor will probably offer you endometrial ablation (burning off the lining of the womb) or transcervical resection of the endometrium (TCRE).

Complex atypical

Usually, your doctor will advise a complete [hysterectomy](#) (removal of the womb, fallopian tubes and ovaries, or TAHBSO) for complex atypical hyperplasia because there is a 30% chance it could develop into cancer of the uterus. Your doctor may also wish to dissect your pelvic lymph nodes if he or she suspects cancer is present and has spread (metastasized). Your doctor may want to thin out

your endometrium before the surgery, to make your uterus easier to remove through your vagina, so you may be offered male hormones, which will send you into menopause. Removal of the ovaries ([oophorectomy](#)) will require hormonal therapy support to address the resultant deficiencies of [estrogen](#) and [testosterone](#).

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 metabolized 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 brandnames and is commonly used to treat heavy menstrual

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TESTOSTERONE www.androfeme.com

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 postnatal depression. MPA increases the risk of blood clots, especially in smokers, can cause depression, suicidal feelings, and dementia. 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.

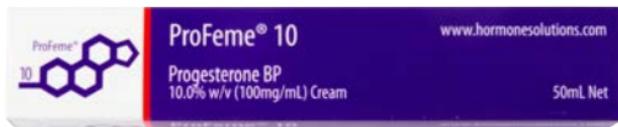
Progesterone receptors in the body are extremely fussy as to what “key” switches them on. Progestins such as MPA do not interact with the progesterone receptor in the same way that bio-identical progesterone does and therefore the estrogen-dominant symptoms do not respond to a progestin in the same way it does to natural progesterone.

PROFEME® progesterone cream ([Lawley Pharmaceuticals](#), Australia) contains the hormone progesterone identical to that which is produced by the ovary – natural progesterone cream is an effective, reliable mode of administration of progesterone for the management of **simple hyperplasia**. Other delivery methods of natural hormones, such as lotions, gels, sprays and troches, have not proven to be as effective for the management of simple endometrial hyperplasia.

If within 3 months of initiating treatment with PROFEME® 10% progesterone cream significant improvement is not seen in simple endometrial hyperplasia with stabilization of periods and reduced endometrial thickness then a synthetic progestin should be considered by your doctor. The other more complex forms of endometrial hyperplasia require more detailed interventions than natural progesterone treatment.

Wild yam treatments sold in health food stores contain a steroid substrate called diosgenin, which is chemically similar to

progesterone, but does not act like progesterone within the body. Humans cannot convert diosgenin into progesterone – a point often misrepresented by marketers of wild yam products. Wild yam treatments are **totally ineffective** in managing any form of endometrial hyperplasia.



What is the role of progesterone in women?

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.

LAWLEY PHARMACEUTICALS www.lawleypharm.com.au

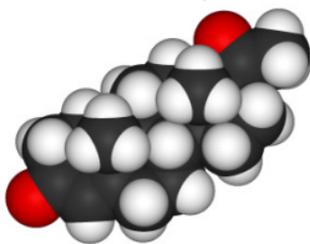
PREGNANCY www.understandingpregnancy.biz

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.

Women use progesterone to prevent [excessive menstrual bleeding](#) and to assist with in-vitro fertilization. A woman who is prone to [miscarriage](#) (**especially repeat first-term miscarriages**) can use progesterone to help maintain her pregnancies, because it reduces pre-term births and the time babies spend in neonatal intensive care units.



Progesterone molecule

[Mood changes](#), [anxiety](#), [depression](#), [weight gain](#), [irregular periods](#), [headache](#), [migraine](#), [infertility](#), [miscarriage](#), [premenstrual syndrome \(PMS\)](#), [post partum depression](#), [endometriosis](#), [pregnancy problems](#), [breast disorders](#) and [polycystic ovarian syndrome \(PCOS\)](#) are some of the medical conditions associated with reduced progesterone production.

The Progesterone Deficiency Assessment Questionnaire

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 that they steadily get worse with time which often leads women to seek medical intervention. Endometrial hyperplasia may be one of numerous other symptoms associated with progesterone deficiency.

EXCESSIVE MENSTRUAL BLEEDING

www.understandingheavyperiods.com

MISCARRIAGE www.understandingmiscarriage.com

MOOD CHANGES www.understandingmoodchanges.com

ANXIETY www.understandingestrogendominance.com

DEPRESSION www.understandingestrogendominance.com

WEIGHT GAIN www.understandingestrogendominance.com

IRREGULAR PERIODS www.understandingperimenopause.com

HEADACHE www.understandinghormonemigraine.com

MIGRAINE www.understandinghormonemigraine.com

INFERTILITY www.understandinginfertility.biz

PREMENSTRUAL SYNDROME (PMS)

www.understandingpremenstrualsyndrome.com

POST PARTUM DEPRESSION

www.understandingpostpartumdepression.com

ENDOMETRIOSIS www.understandingendometriosis.com

PREGNANCY PROBLEMS www.understandingpregnancy.biz

BREAST DISORDERS www.understandingbreastdisorders.com

POLYCYSTIC OVARIAN SYNDROME (PCOS)

www.understandingpcos.com

The Progesterone Deficiency Assessment Questionnaire allows for a baseline assessment of symptoms to be made and provides a valuable tool for the monitoring of whatever method of symptom management a woman chooses to undertake. This results of the questionnaire do not give any direct guide about the severity or degree of the endometrial hyperplasia, however it can provide insight into the degree of progesterone deficiency and how other symptoms are related to the underlying condition of progesterone deficiency causing the endometrial hyperplasia.

The Progesterone Deficiency Assessment Questionnaire is a 15 question self-assessment tool women can use to assess the severity of their symptoms and can be taken online at <http://www.hormonesolutions.com.au/PDA>. 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"/>
Fatigue/lack of energy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Decreased concentration/alertness /memory loss	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Urinary Incontinence	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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 that they can cause symptoms similar to the feeling of pregnancy:

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

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

For comprehensive information on the safe and effective use of progesterone in women view www.hormonesolutions.com.au or download the booklet below.



What about homeopathic and herbal treatments?

Homeopathy is a complementary therapy. Homeopaths claim that like cures like. Essentially, homeopaths believe that 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 progesterone, nor have they been demonstrated to cause any change in progesterone levels.

Homeopathic and herbal treatments are definitely NOT suitable or effective in treating endometrial hyperplasia.

How do I use PROFEME® progesterone cream?

The aim of treatment with PROFEME® progesterone cream is to mimic the body's normal natural hormone production as much as possible. PROFEME® dose applicators are marked in 0.5ml doses. You must tailor the strength, amount and the number of days you apply the cream to your individual requirements. Your doctor or health care professional may alter the dose recommended in this booklet.

Women's hormonal cycles are more complex than the hormone profile of men.

PROFEME® 3.2% progesterone cream is used to control the symptoms of [benign breast disorders](#) during [premenstrual syndrome \(PMS\)](#), [menopause](#), and [peri-menopausal symptoms](#). PRO-FEME® treats other progesterone-deficiency conditions, such as surgical menopause from [hysterectomy](#), [ovarian cysts](#), [uterine fibroids](#) and [fibrocystic breasts](#). If you have had a hysterectomy, the doctor may prescribe estrogen-only for menopausal symptoms to manage [hot flashes](#) and [night sweats](#). In hysterectomized women it is very important that unopposed estrogen must be supported with natural progesterone to prevent symptoms of [estrogen dominance](#).

PROFEME 10% progesterone cream is used to manage more severe progesterone deficiency conditions including endometrial hyperplasia, endometriosis, post partum depression and miscarriage.



Each tube of PROFEME® is supplied with a graduated dose measuring applicator.

BENIGN BREAST DISORDERS

www.understandingbreastdisorders.com

PREMENSTRUAL SYNDROME (PMS)

www.understandingpremenstrualsyndrome.com

MENOPAUSE www.understandingmenopause.biz

PERI-MENOPAUSAL SYMPTOMS

www.understandingperimenopause.com

HYSTERECTOMY www.understandinghysterectomy.com

OVARIAN CYSTS www.understandingovariancysts.com

UTERINE FIBROIDS www.understandinguterinefibroids.com

FIBROCYSTIC BREASTS www.fibrocysticbreastdisease.org

HOT FLASHES www.understandinghotflashes.com

NIGHT SWEATS www.understandingnightsweats.com

ESTROGEN DOMINANCE

www.understandingestrogendominance.com

Recommended starting doses for using PROFEME® natural progesterone cream are as follows:

- **Peri-menopausal women.** Apply 1ml of PROFEME® 3.2% cream via measured applicator (32mg progesterone) daily or in divided doses from day 12-26 of each menstrual cycle. If a menstrual period starts prior to day 26 cease using PROFEME® and consider the first day of bleeding as Day 1 of the new cycle. This is a common occurrence when initiating treatment in peri-menopausal women and should be considered a sign that the treatment is having a positive effect. Symptoms abate in 2nd or 3rd month of use.
- **Pre-menstrual syndrome (PMS).** Apply 1ml of PROFEME® 3.2% cream via measured applicator (32mg progesterone) daily or in divided doses from day 12-26 of each menstrual cycle. Significant alterations to this dosage may be made to achieve a crescendo effect 4-5 days prior to menses. Symptoms abate in 2nd or 3rd month of use.
- **Pre-menstrual dysphoric disorder (PMDD).** Apply 0.5 - 1ml of PROFEME® 10% cream via measured applicator (50-100mg progesterone) daily or in divided doses from day 12-26 of each menstrual cycle. Significant alterations to this dosage may be made to achieve a crescendo effect 4-5 days prior to menses. Symptoms abate in 2nd or 3rd month of use.
- **Endometriosis, Endometrial Hyperplasia and Postpartum depression.** Apply 1.0 - 2.0ml of PROFEME® 10% cream via measured applicator (100-200mg progesterone) daily or in divided doses depending upon the severity of the condition. In reproductive cyclical women initiate treatment on a day 12-26 basis, but this may need to be increased to three weeks use in every four if symptoms/pain emerge upon withdrawal.
- **Infertility/Repeated First-term Miscarriage.** Luteal phase and first trimester corpus luteal support. Apply 1ml of PROFEME® 10% cream (100mg progesterone) daily or in divided doses via measured applicator from day 12-26 of each cycle until pregnancy is confirmed and then 1-2ml daily on a continuous basis until at least week 13 or until full term.

Before conceiving, a woman prone to miscarriage should use PROFEME® 3.2% cream from days 12 to 26 of the cycle until the pregnancy is confirmed. If spotting occurs at week 6 or 7 of pregnancy, a high dose of 100 to 200 mg progesterone cream (PROFEME® 10%) twice or three times daily. Often, women use PROFEME® natural progesterone cream until the baby is full term (40 weeks of gestation).

Note: Amount and duration of application for all conditions must be tailored to individual requirements

PRO-FEME® 10% [Prescribing Information](#) and [Consumer Medicine Information](#) can be downloaded from www.understandingprofeme.com



Why is PROFEME® progesterone cream the best?

If one Googles “natural hormone cream”, “progesterone cream” or “testosterone cream” there are dozens of products claiming to be the “best” and “authentic” natural progesterone/testosterone creams or gels. Just how does one determine which product is most suited to his/her requirements? The following is an outline of basic manufacturing processes to help you decide. The three quality standards of natural progesterone cream are:

1. **Pharmaceutical Grade:** The manufacturer operates to international standards of Good Manufacturing Practice (GMP). GMP means all production processes are standardized and controlled from the time the raw material is procured through to the expiry date printing on

the finished product. The Australian government, like the U.S. and European regulators, enforces rigid government controls on the manufacturing facility, its equipment, processes, and packaging. PROFEME® natural progesterone creams are guaranteed stable, effective, and potent and the world's only pharmaceutical grade progesterone cream. The final product has detailed documentation and is backed by clinical trials that substantiate its therapeutic claims.

2. **Cosmetic Grade:** This is the quality sold over-the-counter in drug, department and grocery stores. Cosmetic grade products do not undergo the rigorous checking processes as is required of pharmaceuticals. Often, brand-names have exactly the same ingredients as generics, just with a different label. Cosmetic grade products are allowed a high bacterial content, so their shelf-life is very limited (usually 3 to 6 months). Cosmetic manufacturers are not required to register their products with the government regulators because cosmetic products do not require clinical trials to prove their worth. Cosmetic grade production is a self-regulating industry.
3. **Compounded Product:** Natural health products from pharmacists, herbalists, homeopaths, naturopaths, and practitioners of traditional Indian and Chinese medicines are compounded. This means the product is tailored to the patient's individual needs in the delivery system most desired. Pharmacists compound drugs that are not commercially available, or in a different strength than that readily available. A compounded product may be needed to make a drug palatable. A compounded product may be needed if the patient reacts to dyes, preservatives, and allergens found in commercial products. Compounded products do not undergo any form of production control, concentration, impurity, stability or efficacy testing. Safe shelf-life is usually extremely short, if at all known. Compounded items are time-consuming to make, so generally they are more expensive.

The only pharmaceutical grade natural hormone creams available worldwide are those made by Lawley Pharmaceuticals, Australia.

Lawley Pharmaceuticals (www.lawleypharm.com.au) makes **PROFEME**[®] 3.2% and 10% progesterone cream for females, **ANDROFORTE**[®] 2 and **ANDROFORTE**[®] 5 testosterone cream for males, **ANDROFEME**[®] 1% testosterone cream for women and **NATRAGEN**[®] estradiol cream for women.

PROFEME[®] progesterone creams are specifically targeted for use in women with declined or lowered serum progesterone levels due to genetic disorders, surgical or chemical interventions, under-production by the ovaries or ageing. Applied topically to the skin, **PROFEME**[®] Progesterone creams for women are the world's only clinically trialled and tested pharmaceutical grade progesterone creams using natural bio-identical progesterone. **PROFEME**[®] progesterone creams are listed with the Australian government (AUST L 95334 / L 70886).

ANDROFORTE[®] 2, **ANDROFORTE**[®] 5 and **ANDROFEME**[®] are testosterone creams specifically targeted for use in men and women with declined or lowered serum testosterone levels due to genetic disorders, neurological disorders, surgical or chemical interventions or under-production by the testes or ovaries and/or adrenal glands. Applied topically to the skin, **ANDROFORTE**[®] 2, **ANDROFORTE**[®] 5 and **ANDROFEME**[®] are the world's only clinically trialled and tested pharmaceutical grade testosterone creams using natural bio-identical testosterone.

ANDROFORTE[®] 2, **ANDROFORTE**[®] 5 and **ANDROFEME**[®] testosterone creams are listed with the Australian government (AUST L 166239 / AUST L 166238 and AUST L 169317 respectively).

PROFEME[®] www.profeme.com

ANDROFORTE[®] 2 www.androforte.com

ANDROFORTE[®] 5 www.androforte.com

ANDROFEME[®] www.androfeme.com

NATRAGEN[®] www.natragen.com

NATRAGEN® estradiol cream for women is specifically for conditions of estrogen deficiency conditions including short-term use for menopausal symptoms not responsive to PROFEME® such as hot flashes, night sweats, vaginal dryness and atrophy. (AUST L 169397)

PROFEME® progesterone cream for women - Quick Q & A

Q. What is meant by the term bioidentical hormones?

A. The term bio-identical hormones refers to the identical hormones to that produced naturally by the ovaries in women and the testes in men. The bio-identical hormone progesterone has the exact chemical finger print as that which is made by the human ovaries. Many pharmaceutical hormones are not bio-identical hormones, but rather synthetic analogues which may have similar actions as bio-identical hormones. In the case of synthetic progestins (progesterone analogues) they do not have the wide spectrum of action as bio-identical progesterone, they are usually stronger and have beneficial actions limited to the uterine lining, they have unwanted side effects compared to the bio-identical hormone progesterone and are patented.

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

A. Yes. PROFEME® progesterone cream is guaranteed 100% to contain ““natural” progesterone. Natural progesterone was the term coined by US doctor John Lee MD to differentiate between the chemical structure of progesterone produced by the ovaries (“natural”) and the chemical structures of the synthetically produced progestins which are often confused as being 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.** Why is PROFEME® progesterone cream superior than other progesterone cream brands?
- A.** PROFEME® progesterone cream is manufactured to pharmaceutical grade standards whereas in the USA over-the-counter progesterone creams are made to cosmetic grade standards. The requirement for labeling disclosure of the amount of progesterone in the finished product is optional. Many products available in the US for example may claim to have progesterone in the finished product, but in fact can have little or no progesterone. Because PROFEME® has much stricter standards of manufacture the amount stated on the label is guaranteed to be what is in the finished product. Additionally PROFEME® progesterone cream has undergone comprehensive raw material purity testing, clinical trials and stability testing. The quality difference between PROFEME® progesterone cream and other cosmetic brands is significant.

- Q.** How long before PROFEME® progesterone cream helps my endometrial hyperplasia?
- A.** Usually it takes between 12-16 weeks for PROFEME® to reduce the thickness of the endometrial lining. Many people want an overnight cure to the problem. It must be remembered that the underlying hormone imbalance that led to the point where endometrial hyperplasia warranted treatment usually developed over many months, if not years. They cannot be reversed overnight. Most people find that the hyperplasia and progesterone deficiency symptoms improve steadily with each month of use. After about 12 months use maximum effect is achieved.

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.

The Lawley Pharmaceuticals portfolio of products include:

ANDROFEME® 1% testosterone cream for women



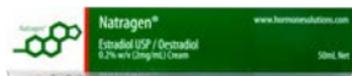
ANDROFORTE® 2% and ANDROFORTE® 5% testosterone cream for men



PROFEME® 3.2% and PROFEME® 10% progesterone cream for women



NATRAGEN® 0.2% estradiol cream for women



Our Mission Statement

Lawley Pharmaceuticals (www.lawleypharm.com.au) strives to provide the optimal delivery systems for the administration of naturally occurring hormones to counter endocrine deficiency states.

Our philosophy is based on the principle to use a bio-identical hormone in preference to a synthetic hormone analogue (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 centres 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 ANDRO-FEME® 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.*

Internet Education Reference Sites

ANDROFORTE www.androforte.com

ANDROFEME www.androfeme.com

PROFEME www.profeme.com

NATRAGEN www.natragen.com

HORMONE SOLUTIONS www.hormonesolutions.com.au

HORMONE SOLUTIONS www.hormonesolutions.com

ANDROPAUSE www.understandingandropause.com

ANOVLUTION www.understandinganovulation.com

BENIGN BREAST DISEASE www.understandingbenignbreastdisease.com

BREAST DISEASE www.understandingbreastdisease.com

BREAST DISORDERS www.understandingbreastdisorders.com
CASTRATION www.understandingcastration.com
DYSFUNCTIONAL UTERINE BLEEDING
www.understandingdysfunctionaluterinebleeding.com
DYSMENORRHEA www.understandingdysmenorrhea.com
DYSPAREUNIA www.understandingdyspareunia.com
EARLY MENOPAUSE www.understandingearlymenopause.com
ENDOMETRIAL HYPERPLASIA
www.understandingendometrialhyperplasia.com
ENDOMETRIOSIS www.understandingendometriosis.com
ESTROGEN DOMINANCE www.understandingestrogendominance.com
FEMALE SEXUAL DYSFUNCTION
www.understandingfemalesexualdysfunction.com
FIBROCYSTIC BREAST DISEASE
www.understandingfibrocysticbreastdisease.com
FSD www.understandingfsd.com
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HYSTERECTOMY www.understandinghysterectomy.com
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KLINFELTER SYNDROME www.understandingklinefeltersyndrome.com
LIBIDO www.understandinglibido.com
LOW LIBIDO www.understandinglowlibido.com
LOW TESTOSTERONE www.understandinglowtestosterone.com
MENOPAUSE www.understandingmenopause.biz
MENORRHAGIA www.understandingmenorrhagia.com

MISCARRIAGE www.understandingmiscarriage.com

MOOD CHANGES www.understandingmoodchanges.com

NIGHT SWEATS www.understandingnightsweats.com

OOPHORECTOMY www.understandingoophorectomy.com

OVARIAN CYSTS www.understandingovariancysts.com

PCOS www.understandingpcos.com

PERIMENOPAUSE www.understandingperimenopause.com

PMDD www.understandingpmdd.com

POLYCYSTIC OVARIAN SYNDROME

www.understandingpolycysticovariansyndrome.com

POST NATAL DEPRESSION www.understandingpostnataldepression.com

POST PARTUM DEPRESSION

www.understandingpostpartumdepression.com

PREGNANCY www.understandingpregnancy.biz

PREMENSTRUAL SYNDROME

www.understandingpremenstrualsyndrome.com

UTERINE FIBROIDS www.understandinguterinefibroids.com

SYMPTOM TRACKER

Check off your symptoms ✓

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Period = P														
Acne														
Anxious/ Depressed														
Appetite Change														
Backache														
Bloating														
Breasts Tender														
Can't Concentrate														
Constipation														
Cramps														
Diarrhea														
Disturbed Sleep														
Food Craving														
Headache														
Joint/Muscle Pain														
Moody/Crying														
Poor Memory														
Tense/Irritable														
# of pads used														
Other														

Yes, I think I ovulated on Day ____ No, I think I did not ovulate this cycle ____														
Day	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Period = P														
Acne														
Anxious/ Depressed														
Appetite Change														
Backache														
Bloating														
Breasts Tender														
Can't Concentrate														
Constipation														
Cramps														
Diarrhea														
Disturbed Sleep														
Food Craving														
Headache														
Joint/Muscle Pain														
Moody/Crying														
Poor Memory														
Tense/Irritable														
# of pads used														
Other														

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LAWLEY

Hormone Solutions