

Understanding benign breast disorder



LAWLEY

Hormone Solutions

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What is benign breast disease?

Benign breast disease (BBD) means a breast disorder that is not cancerous and is usually not life threatening. A malignant disease is cancerous. Benign does not mean the disease is painless or that tissue damage does not occur from abnormal growth that crushes healthy tissue. Types of benign breast disease include:

Early breast cancer is usually painless.

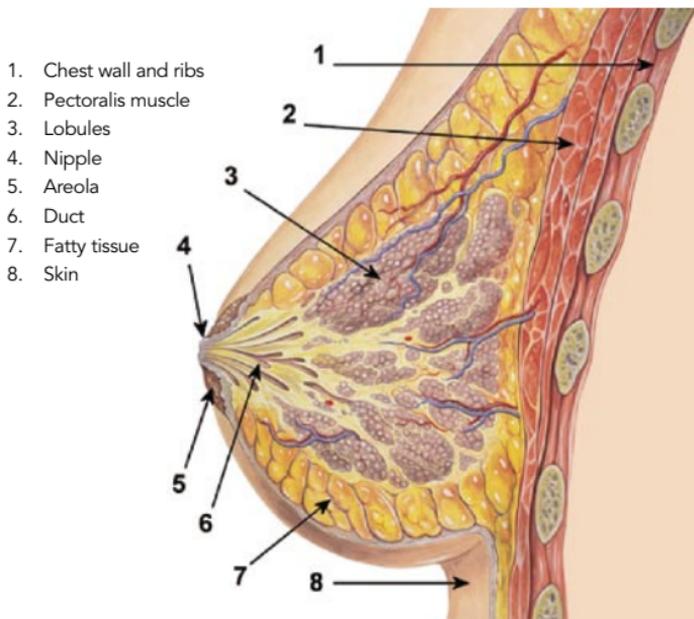
- Mastalgia, breast pain from hormonal changes
- Fibrocystic breast disease
- Mastitis from infections, such as thrush in nursing mothers
- Sclerosing adenosis, hardened breast glands
- Fatty necrosis, scar tissue that replaces injured breast fat
- Galactorrhea, abnormal milk production
- Noncancerous breast tumors
- Gynecomastia, female breast growth in males

This booklet concentrates on female benign breast disease.

If you are male, please read Lawley Pharmaceutical's Understanding Gynecomastia booklet, available from our Web site at:

www.understandinggynecomastia.com

Normal Breast Structure



When a girl reaches puberty, her breasts enlarge if her brain and glands are all working in concert – hypothalamus, anterior pituitary, ovaries, pancreas and thyroid. A normal female breast weighs between 50 to 500 grams (1.76 to 17.63 ounces). Here's a simplified explanation of how the breast is formed and operates, so you can easily understand your particular problem and treatment options:

- Each breast is divided into 15 to 20 lobes
- Lobes divide into smaller lobules
- Lobules end in milk-producing bulbs, also called terminal ductal lobular units (TDLU)
- Lobes, lobules and bulbs are connected by ducts
- Ducts lead to the nipple, where milk is expressed

- Fat fills the space between lobules and ducts
- The areola is the pink or dark ring around the nipple, which has oil glands to lubricate the breast for nursing
- No muscle is within the breast, just underneath it, riding atop the ribs
- Lymph nodes in the armpits, skin and chest wall drain the breasts of excess fluid and potential disease organisms

Your breasts change five times throughout the course of your menstrual cycle. Three or four days before menstruation, they retain water and the cells proliferate under the influence of estrogen and progesterone. Day 1 of your menstrual cycle is the first day you bleed. During the first two weeks of your cycle, estrogen causes the ducts in your breasts to grow. During the last two weeks of your cycle, progesterone causes the lobes to grow.

If you conceive, progesterone lays the foundation for milk production and breastfeeding (lactation) by the fifth or sixth month of pregnancy. The hormones required for breastfeeding are follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, oxytocin (for “let-down” reflex), and human placental lactogen (HPL).

Breasts enlarge and the areola darkens for breastfeeding.

Breasts lose volume (involute) during menopause. If you are thin, breastfeeding, or have small breasts, then the fat, lobes, and underlying muscle can make your breasts seem lumpy, when they are really quite normal.

How do I find breast disease?

Know what is normal for your breasts through monthly breast self-examinations (BSE). You can perform a BSE while standing in the shower, or reclining in bed with a pillow behind your shoulder, or in front of a mirror. Reclining propped on a pillow distributes the breast tissue most evenly, so it is easier to find small lumps. Soap and water reduce friction, making your fingers more sensitive. The mirror will show colour changes, and side-lighting will show irregular texture. Use whichever position is easiest and most convenient for you.

Bend your left arm and cup the back of your head with your left hand. Gently feel your left breast with the pads of the three middle fingers on your right hand, using either a concentric circle or pie-wedge pattern. Feel the chest from the collarbone to the ribs just below your breasts. Include the breastbone and armpit, too. Go over each area again with medium pressure and then firm pressure. Switch sides. Look for prominent veins, drainage from the nipples, redness, bulges, white scales, pigment changes in moles, persistent sores, indentations, “orange peel” skin, flattening, inverted nipples or nipples pointing in a direction that is not usual for you. These could indicate tumor growth. Bend over a chair and let your breasts hang. If your breast contour is distorted and your breasts do not fall freely away from your torso, then a Cooper’s ligament could have a growth impinging on it. If you find an abnormality, remember that 9 out of 10 women will never develop breast cancer.

When should I be concerned?

- If you are in your childbearing years and are not pregnant or breastfeeding, see your doctor if your breast pain or changes last more than one *menstrual* cycle.
- If you are breastfeeding, suppressing your milk after delivery, or recently miscarried, and experience flu-like symptoms, fever over 38.5°C (101°F), and a sore, red, hardened breast, seek medical attention *within 8 hours*.
- If you are postmenopausal and experience breast pain of any duration, see your doctor immediately.
- Whitish or clear nipple discharges are not always abnormal, but *always* get a bloody discharge evaluated by a doctor as soon as possible. Bring a sample of the discharge with you in a sterile container, if you can.
- If you have an enlarged vein under the nipple, perhaps with a groove beside it, you could have Mondor’s disease, which your doctor monitors for 12 weeks

What are the signs and symptoms of breast cancer?

Early breast cancer is usually painless, so your breast discomfort is actually reassuring.

Seek medical attention if you have these signs and symptoms:

- Persistent breast lumps or swelling that do not resolve when your menstruation is finished
- Inverted nipple
- Bloody nipple discharge
- Changed breast shape
- Dimpled or puckered breast skin
- Scaly skin, especially ringing the nipple

What causes benign breast disease?

Mastalgia

Mastalgia is diffuse breast pain due to hormonal fluctuations, which predictably affects:

- Newly pregnant women
 - Mothers three days after delivery
 - Newborn babies
 - Birth control pill users
 - Menopausal women who take estrogen based hormone replacement therapy (HRT)
 - Women with premenstrual syndrome (PMS)
(See www.premenstrual-syndrome.info)
 - Pubescent boys around age 14 with normal pubertal hypertrophy
- Mastalgia is due to breast growth, and produces overall tenderness, rather than pain in a localized area. Mastalgia can occur with all of the following, more serious breast conditions.

Fibrocystic breast disease

Fibrocystic breast disease is liquid-filled cysts caused by an imbalance between the hormones estrogen and progesterone. Cysts can be too tiny to feel, or can be several inches across and easily found with an ultrasound. Near the skin's surface, fibrocystic breasts feel soft, but the deep tissue feels lumpy or ropey. The cyst can be irregularly shaped. Your doctor may also call it **mammary dysplasia**, or **chronic mastitis**, or **generalized breast lumpiness**. Pain from fibrocystic breast disease is usually a burning sensation localized near the armpit, or around the areola and nipple. The breasts feel heavy and tender, especially during the second half of the menstrual cycle, when excess fluid collects in the breasts. Often fibrocystic breast disease arises upon commencing an estrogen based oral contraceptive or if already present, exacerbated by using the Pill. During pregnancy, when hormones stimulate milk production, women with fibrocystic breast disease often find their condition is aggravated. As women approach middle age, their breasts become lumpier because the milk-producing tissue shrinks and the fat content increases. Fibrocystic breast disease dissipates completely after natural menopause, when breast size decreases. However, if the woman takes a higher dose estrogen replacement therapy, fibrocystic breast disease can worsen.

Mastitis

Mastitis is breast inflammation. In **women of childbearing years**, mastitis is usually from an infection contracted through improper nursing technique. A baby who cannot latch properly is apt to inadvertently damage the nipple. Milk pools in the lobes. Tiny cracks in the skin allow micro-organisms into the breast. The infection can be bacterial, viral, or fungal (thrush). The breast is hot, hard, red and swollen, often with foul-smelling green or yellow pus leaking from the nipple. Pain is often localized to a specific milk duct in one breast, and is intense or stabbing. Mothers who bottle feed and allow their breasts to become engorged with milk also develop mastitis. **Ectasia** occurs when the milk ducts shorten and widen as a result of normal ageing. In **menopausal women**, mastitis is caused by mammary duct ectasia. A lump of scar tissue can sometimes be felt behind the nipple, which eventually can invert the nipple. The milk ducts are clogged, inflamed, and secrete a greenish-grey discharge.

Sclerosing adenosis

These are the growths most commonly found by women during breast self-examination. Your doctor may also call adenosis a **fibroadenoma**. Fibromas are overgrowths of fibrous connective tissue that support the breast. Adenomas are painless glandular masses from overgrowth of the lobes, which feel like a solid, rubbery ball about 1 to 3 centimeters in diameter. Adenosis is called “breast mouse” because it can be easily moved around. Unlike fibrocystic breast disease, which often has an irregularly shaped cyst, adenosis is smooth and round, with a clear-cut shape. If you develop adenosis, it means you are especially sensitive to the hormone estrogen. Hence, if you are a teenager, using an estrogen based oral contraceptive, pregnant, or breastfeeding, expect your adenosis to enlarge. Rarely does an adenosis grow to 5 cm. Often, adenosis (fibroadenoma) causes greenish nipple discharge.

Fatty necrosis

Obese, middle-aged women who have large, pendulous breasts are prone to develop lipid cysts that calcify and break down over time. Fatty necrosis is literally a calcium soap deposit. Your doctor may also refer to it as **steatonecrosis**. Unlike the fluid-filled cysts of fibrocystic breast disease, fatty cysts are solid, hard, round, and painless. Their size does not fluctuate with the menstrual cycle. The area usually affected is around the areola (darkly colored ring around the nipple). It may look like a bruise. Fatty necrosis is especially likely to occur in women who have had: A seat belt injury; blunt trauma; breast reduction; radiation therapy; a breast implant removal; lumpectomy; biopsy; hyperactive parathyroid glands; or who use the blood thinner warfarin (Coumadin®, Marevan®).

Galactorrhea

Galactorrhea is an inappropriate, large amount of milk or colostrum (clear or cloudy, slippery pre-milk) leaking from your breasts, when you are neither pregnant nor breastfeeding. Galactorrhea occurs when you produce too much prolactin hormone. Women and men who take prescription medication or over-the-counter herbs can unwittingly induce galactorrhea. Check your medicine cabinet for these likely suspects known to produce galactorrhea as an unwanted side-effect:

| DRUG | FUNCTION |
|---|--|
| Claritin® | Antihistamine |
| Famotidine, ranitidine, cimetidine | Antacids for stomach ulcers |
| Oral birth control pills, Depo-Provera® medroxyprogesterone injections, PremPro® | Contraceptives and hormones |
| Reserpine, Aldomet®, atenolol, verapamil | Control high blood pressure |
| Brewer's yeast | B vitamin tablets, beer |
| Antidepressants | Fluoxetine, Paroxetine, Sertraline, Citalopram |
| Amphetamines | Street drug and diet aid for appetite suppression |
| Isoniazid | Tuberculosis treatment |
| Cyclobenzaprine (Flexeril®) | Muscle relaxant for injuries |
| Sumatriptan® | Migraine headache treatment |
| Valproic acid (Depokene®, Epilim®) | Anticonvulsant to prevent seizures |
| Phenothiazines, chlorpromazine, prochlorperazine | Psychiatric drugs (sedatives, tranquilizers, antipsychotics and anti-schizophrenics) |
| Fenugreek, anise, fennel, hops, nettles, red clover, red raspberry, and blessed thistle | Galactagogue herbs to increase milk production in new mothers and reduce menopausal symptoms |

Galactorrhea can also result from: A brain injury; irritation of the chest wall (e.g., breast implant, dermatitis, shingles, burns, ill-fitting clothes); a deficient thyroid gland in the neck (hypothyroidism); tuberculosis; swelling of the brain, often from infectious mosquitoes (encephalitis); Cushing syndrome; acromegaly; nerve disorders; Hodgkin's disease; hydatiform mole; kidney or bronchial cancer; or a tumor in the pituitary gland of the brain. It almost always affects both breasts. Newborn babies often have galactorrhea (witches' milk) for a couple of weeks after birth, through exposure to their mothers' hormones, and this resolves spontaneously without medical treatment. Pubescent boys may notice rudimentary breast

development and experience mild galactorrhea. Like newborns this is normal and symptoms resolve spontaneously. Galactorrhea can also be idiopathic, meaning it has no known cause.

Noncancerous breast tumors

A tiny amount of blood can occasionally be expelled from the breast with the milk during normal breastfeeding. However, significant bloody discharge from a nipple can indicate an **intraductal papilloma** is present, which is a benign (noncancerous) tumor in the milk duct that is nevertheless painful. Women near menopause most likely develop one lone papilloma (warty growth) near the nipple of one breast only, which bruises or bleeds when bumped or rubbed even slightly. Young women tend to develop papillomae in both breasts.

A rare form of breast tumor that starts out benign and can develop into cancer subsequently is phyllodes tumor. Your doctor may want to perform a **core biopsy** in hospital to confirm suspected phyllodes, rather than perform **fine needle aspiration cytology** (FNAC) in the office. Phyllodes are persistent, so even if your doctor surgically removes the tumor, it can recur. You require a mammogram every two years to detect recurrence early. Your doctor may suggest a **mastectomy**, or breast removal, followed by **breast reconstruction** to restore a normal appearance.

Who develops benign breast disease?

If you took conjugated equine estrogen (e.g., Premarin®) to control your menopausal symptoms, you have double the risk of developing benign breast disease.

Fibrocystic Breast Disease

About 30% of adult women have fibrocystic breast disease, characterized by fluid retention, hard lumps and fluid-filled cysts. Women 35 to 50 years of age are most likely to be affected.

Mastitis

About 1 in 20 women develop mastitis. Most are first-time mothers. The most frequent time mastitis develops is from Day 10 to Day 28 postpartum. Menopausal women often develop duct ectasia as a result of rapid hormonal fluctuations.

Sclerosing adenosis

Women in their teens and early twenties (especially oral contraceptive users) and Black women are most likely to develop adenosis (fibroadenoma). Pregnant and nursing mothers have larger adenosis.

Fatty necrosis

About 31% of obese women who receive breast-sparing irradiation therapy for cancer develop fatty necrosis or inflamed fat in their breast tissue, evidenced by dimpled skin. It is usually of no consequence.

Galactorrhea

One-quarter of all women experience inappropriate breast milk production at some time in their lives.

Noncancerous breast tumors

Women with breast hyperplasia (tissue overgrowth) may go on to develop cancer. The first sign is atypia (abnormal cells) found on fine needle aspiration biopsy (FNA).

How dangerous is benign breast disease?

Fibrocystic breast disease makes it difficult for your doctor to detect true cancer. It minimally increases your chance of developing breast cancer.

Left untreated, **mastitis** can develop into a dangerous abscess that can cause blood poisoning (sepsis). Although you may be reluctant to take antibiotics or antifungals, they are absolutely necessary.

Sclerosing adenosis, intraductal papilloma, and duct ectasia do not increase your chances of breast cancer.

Fatty necrosis closely mimics breast cancer, so it is essential that your surgeon performs a core needle biopsy before removing your breast (mastectomy) unnecessarily. Fatty necrosis does not increase your risk of developing cancer.

How is benign breast disease treated?

First Aid for Mastalgia

Hormone-related breast pain occurs in the second half of the menstrual cycle and resolves without treatment when the menstrual period is over. If it is particularly acute:

1. Take acetaminophen (Tylenol[®], paracetamol) or an NSAID (aspirin, Motrin[®]). Never use aspirin (acetylsalicylic acid or ASA[®]) for a child under 19 who has a fever of viral origin. Children can develop Reyes syndrome, a rare but deadly form of brain and liver damage, from aspirin exposure.
2. Apply cold compresses. Place ice in a plastic bag and wrap it in a towel. Never allow ice to rest directly on the breast, because frostbite can occur. Hold the cold compress gently over the breast for a maximum of 20 minutes. Allow the breast at least 20 minutes to recover from the chilling.
3. Avoid caffeine
4. Take evening primrose oil and Vitamin E

See your doctor if the breast swelling does not resolve in two weeks, or if it recurs again next menstrual cycle.

Most cases of gynecomastia in children do not require treatment. Your doctor will probably adopt a “watchful waiting” approach for one or two years, in the hope that the child’s hormones will settle without intervention.

Fibrocystic breast disease

Prevention

Ovulation occurs about Day 14 of your menstrual cycle. Applying 20 to 32 mg of natural progesterone cream to your breasts daily from Day 14 to Day 26 of your cycle restores normal breast tissue in three or four months of continued cyclical use. A small maintenance dose is adequate once the breasts are no longer cystic. Supplement your diet daily with 400 to 600 mg of natural Vitamin E, 350 mg of magnesium, and a balanced B complex vitamin tablet. Do not consume high doses of Vitamin B6 alone, as it can cause irreversible nerve damage. Reduce your fat intake to 15% of your total diet and you may experience an improvement over time. A 500 mg daily omega-3 supplement (fish or flax oil) may help. Visit

a qualified bra fitter, and buy two supportive bras to protect your sore breasts in the latter half of your cycle.

Intervention

Most fluid-filled cysts resolve spontaneously without any medical intervention by the end of the menstrual period. However, if your cyst does not drain by itself, or is causing you pain, then the first line treatment is to drain the fluid with a syringe. Cysts will most likely recur with the next menstrual cycle. A surgical biopsy could remove a persistent cyst, but leaves a scar. Remember, this is a disease of your childbearing years. Your symptoms will likely disappear when you enter menopause.

If after three months of natural progesterone cream treatment your fibrocystic breast disease continues to cause you severe pain, then your doctor may offer you either tamoxifen, a drug that prevents breast cancer, or danazol, a synthetic male hormone. These two drugs change the way the female hormones estrogen and progesterone work on breast tissue. However, long-term tamoxifen use can cause uterine cancer, and danazol will put you in an artificial menopause.

Mastitis

Apply warm compresses to encourage milk and discharge to flow out of the breast. Postpartum mastitis is a medical emergency, so see a doctor or nurse practitioner within 8 hours. Do not stop breastfeeding; if your milk is green, express it with a pump. Infected postpartum mastitis and mammary duct ectasia both require prescription antimicrobials. Your doctor takes a swab for the microbiology lab determine if your infection is bacterial, fungal, or viral. If the drainage from your ectasia is not infected, then you do not require treatment, and will likely be told to accept it as a normal part of ageing. If an **abscess** forms, your doctor must lance and drain it. If the ducts remain clogged, then your doctor can perform a **microdochectomy** to remove only the affected ducts, or **Hadfield's procedure** to remove all major milk ducts. Both types of duct removal require general anesthetic and an overnight hospital stay. If you are past childbearing, your doctor may prefer a Hadfield's procedure to prevent a recurrence. Either procedure leaves you with diminished nipple sensation. The scar will be partially hidden by your dark areola.

Sclerosing adenosis

Your doctor measures your adenoma. If it is less than 3 cm in diameter, your doctor performs a fine needle biopsy and sends the drainage to a cytologist for expert examination. Your doctor may suction out small adenomas completely with a mammotone, but will need the help of a radiologist to image the site. If your adenoma is more than 3 cm in diameter and you want it removed, then your doctor must use a scalpel. You will have a small scar that fades over time.

Fatty necrosis

Cysts can be filled with solid lipids (fats and oils) instead of liquid. If you are young, your breast tissue may be too dense for a radiographer to find necrosis with a mammogram; you may require an ultrasound, instead.

Most often, fatty necrosis resolves by itself and does not require treatment. However, if the lump persists or enlarges, you do require aspiration. If you opt for a local anesthetic, then you can be treated as a day patient. If you opt for general anesthetic (unconsciousness), then you must stay in hospital overnight. The doctor inserts a fine needle into the cyst and tries to drain it. If the doctor cannot drain the cyst because it has solidified, he or she will send the cells in the needle to a pathologist for expert examination. The doctor may remove the necrosis with a scalpel, in which case you will have a few stitches. Your nurse demonstrates how to care for them afterwards.

Galactorrhea

Some women start lactating in their second trimester of pregnancy (Week 13 to Week 27) and continue to produce milk for two years after they cease breast feeding. See a qualified bra-fitter and replace your ill-fitting bras and clothing so that your nipples do not receive irritating stimulation. If you are taking body-building hormones, herbs, or prescription medication that causes you to leak milk, the obvious solution is to stop using the offending chemical and consult your pharmacist to find a safe alternative. Your doctor orders a urine test to rule out pregnancy (or cancer of the testicles, if you are a male with gynecomastia- also see www.understandinggynecomastia.com). You also require blood tests for

the pituitary, thyroid, adrenals, kidneys and ovaries at the lab as a standard precaution. If your lab results are normal, the doctor orders a CT or MRI brain scan to rule out a brain tumor.

Treatment depends on whether or not you wish to conceive, and if you experience visual loss. You may be offered bromocriptine, pergolide, cabergoline, or brain surgery. It may take up to two years for your prolactin hormone to normalize, and you require regular blood tests during that time.

Noncancerous breast tumors

Since bloody nipple discharge is a sign of both noncancerous breast tumors and breast cancer, you need a mammogram and breast biopsy to differentiate between the two. Calcifications in your breast, often from irritation by an implant, can foreshadow cancer and are only detectable by mammogram or ultrasound if you are younger than 35 and have dense breasts. If you have a papilloma and the bleeding and constant bruising are bothersome to you, a surgeon can remove the duct containing the papilloma, and still preserve the cosmetic appeal of your breast.

What can I expect at my doctor's visit?

Bring all prescription drugs, herbs, and supplements you are taking with you to your doctor's visit. Be honest with your doctor if you use street drugs like amphetamines that aggravate breast tissue. Your doctor may consult with a pharmacist to find out if your benign breast disease could be the result of a drug interaction.

Be prepared to answer these questions when the doctor takes your history:

- When did you first notice the abnormality in your breast?
- Is there any discharge, and if so, what colour and consistency?
- Have you gained or lost any hair on your chest, underarms or face?
- Do you also have enlarged breasts?
- Does your breast size vary or remain the same?
- At what age did you first start menstruating?
- Do you have children? If yes, how old were you when your first child was born?

- Is there tenderness or pain in your groin, breasts or pelvis?
- Have you ever had your nipples or genitals pierced, and if so, were there complications?
- Do you regularly use prescription or street drugs?
- Do you use herbs or body-building preparations?

Following the history, your doctor performs a physical examination of your breasts and sex organs. You may recline on the examination couch, or the doctor may ask you to reach your hands over your head, or to lean forward with your hands braced on your hips. He or she will specifically look for dimpling, rashes, ulcers, colour changes, and asymmetry in your breasts. Your doctor will suspect **breast cancer** if there is: Breast growth on one side only (unilateral); nipple inversion or flattening; discharge that is not milk (watery, bloody, or pus-streaked); "orange peel" skin; heat or redness; an itching or burning sensation.

Your doctor will feel (palpate) for a mass in your pelvis to find fibroids, cancerous tumors, lesions, discharge, and venereal disease. Your doctor must rule out pregnancy, which turns the cervix blue. If you have not had a pap smear in the past year, the doctor scrapes your cervix with a wooden Popsicle stick, smears the sample on a slide, and sends it to the Pathology Lab for expert examination.

Sexually active females give a urine sample or a β hCG blood test as a routine precaution to ensure they are not pregnant before beginning hormone therapy. This is a standard legal precaution, and is especially important if your periods are irregular.

You may be sent to the Diagnostic Imaging Department for chest and skull x-rays or a mammogram. You may be asked to get a CT, MRI or PET scan, or a biopsy.

The usual preliminary blood tests for benign breast disease include:

| PROFILE | TEST | NORMAL ADULT – NON-PREGNANT – FEMALE VALUE |
|----------|--------------|---|
| Thyroid | T3 | 110 to 230 ng/dL |
| | T4 | 5 to 10 µg/dL |
| | TSH | 1 to 4 µU/mL |
| Liver | AST | 5 to 40 IU/L |
| | ALT | 5 to 35 IU/L |
| | ALP | 30 to 85 IU/mL |
| | Bilirubin | 0.1 to 1.0 mg/dL |
| | Cholesterol | 150 to 250 mg/dL |
| Kidney | Creatinine | 0.7 to 1.5 mg/dL |
| | BUN | 7 to 20 mg/dL |
| Adrenals | Cortisol | 2 to 28 µg/dL depending on time of day |
| | ACTH | 15 to 100 pg/mL |
| Hormones | GH | 0 to 8 ng/mL |
| | FSH | 3 to 20 mIU/mL |
| | LH | <7 mIU/mL |
| | HCG | Negative unless pregnant |
| | Progesterone | <2 ng/mL before ovulation >5 ng/mL after ovulation |
| | Estradiol | Varies from 25 pg/mL on Day 3 to 200 pg/mL at ovulation |
| | Prolactin | < 24 ng/mL |
| | Testosterone | 6 to 86 ng/dL |
| | SHBG | 18 to 114 nmol/L |

These are guidelines only. Children, pregnant women 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. To find out more about diagnostic tests, visit Lab Tests Online: <http://www.labtestsonline.org/understanding/index.html>

What are the pros and cons of natural progesterone treatment versus synthetics?

Natural progesterone creams are absorbed through the skin (transdermally), so they avoid first-pass metabolism by the liver, 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 bioavailability of the hormones by breaking them down into less active forms. Synthetic hormone pills (such as medroxyprogesterone acetate) are rapidly metabolized by the liver on the first pass, so the amount of hormone you receive is reduced. Oral hormones are excreted in the urine, so most of your dose is lost.

PRO-FEME® 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 for the management of **fibrocystic breast disease**. Other delivery methods of natural hormones, such as lotions, gels, sprays and troches, have not proven to be as effective for the management of fibrocystic breast disease.

If within four months of initiating treatment with PRO-FEME® 3.2% progesterone cream significant improvement is not seen in the fibrocystic breasts then other treatment options may be considered by your doctor.

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 breast disorders.

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 (see www.progesteroneinpregnancy.info).

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 molecule

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 one of the hormones that regulate the uterus, gall bladder, thyroid, bones, teeth, skin, ligaments, tendons, and joints.

Women take progesterone to prevent excessive menstrual bleeding and to assist with in-vitro fertilization. A woman with a very short cervix who is prone to miscarriage can take progesterone to help maintain her pregnancies, because it has been proven to reduce pre-term births and the time babies spend in neonatal intensive care units (see www.miscarriage-hormone-treatment.com).

As previously stated, simple endometrial hyperplasia is an estrogen induced overgrowth of the cells lining the wall of the uterus. This is most usually due to natural progesterone deficiency, hence the excessive build up of the endometrial lining.

What are the side-effects of progesterone replacement therapy?

PRO-FEME® natural progesterone cream has very low toxicity. Progesterone is the hormone that supports a pregnancy ('pro' means for and 'gestation' means pregnancy). The most common problems associated with progesterone treatments are that they can cause symptoms similar to pregnancy:

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

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.

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.

The herb Chaste berry (*Vitex agnus castus*) does not contain progesterone, but it may indirectly help you produce progesterone over the course of several months by stimulating your pituitary gland to produce LH. Chaste berry has unpleasant side effects, such as an itchy skin rash, nausea, dry mouth, digestive upset, hair loss, headaches, rapid heartbeat, and bleeding between periods. *Vitex* is called chaste berry and monk's pepper because it was used for centuries to reduce libido. Do not use chaste berry if you are pregnant, breastfeeding, or have endometriosis, fibroids, cancer of the ovaries or breast, schizophrenia, or Parkinson's disease. It is unsafe to take chaste berry in conjunction with these prescription drugs: bromocriptine; cabergoline; carbidopa-levodopa; chlorpromazine; Clozaril®; Haldol®; Mirapex®; oral contraceptives; Reglan®; Requip®; Risperdal®; Seroquel®; thioridazine; trifluoperazine; and Zyprexa®. Inform your doctor and pharmacist that you are taking chaste berry before starting any new medication to avoid adverse drug interactions.

Who should not use natural progesterone cream?

Do not use PRO-FEME® progesterone cream if you have:

- A known allergy or sensitivity to any of the ingredients in the cream, especially macadamia or almond oil
- Yellow jaundice or liver disease
- Undiagnosed vaginal bleeding
- The immune disease herpes gestationis, which develops during pregnancy and is also called pemphigoid gestationis (PG) this is NOT herpes simplex or the common cold sore nor genital herpes
- A clotting disorder, like deep vein thrombosis (DVT)
- Severe heart, blood vessel, or liver disease
- A personal history of carcinoma (cancer) of the breast or endometrium

How do I use natural hormone cream?

The aim of natural hormone replacement therapy is to mimic your body's normal natural hormone production as much as possible. PRO-FEME® dose applicators are marked in unit doses. You must tailor the strength, amount and the number of days you apply the cream to your individual requirements. Your doctor may alter the dose recommended in the directions on the product insert.

Women's hormonal cycles are more complex than the hormone profile of men. PRO-FEME® 3.2% progesterone cream is prescribed to control the symptoms of fibrocystic breast disease and breast disorders during premenstrual syndrome, menopause, and the perimenopause.

The usual dose of PRO-FEME® 3.2% progesterone cream for treating fibrocystic breasts is two units (32mg progesterone) used once daily from day 12-26 of the cycle and review after 3 cycles of treatment.



PRO-FEME® [Prescribing Information](http://www.hormonesolutions.com.au) and [Consumer Medicine Information](http://www.hormonesolutions.com.au) can be downloaded from <http://www.hormonesolutions.com.au> (or by clicking on the hyperlinks).

PRO-FEME® can be an appropriate adjunct therapy for other progesterone-deficiency conditions, like surgical menopause from [hysterectomy](#), [ovarian cysts](#), [uterine fibroids](#), estrogen-dependent malignancies, and [endometriosis](#). If you have had a hysterectomy, the doctor may prescribe estrogen only for menopausal symptoms. This estrogen needs to be supported with natural progesterone to prevent possible estrogen dominance.

Alternatively, you or your doctor may alter your dose to achieve a crescendo effect 4 or 5 days prior to your menstruation. Your doctor may tell you to start with half a unit and step up the dose over the course of three months, depending on your symptoms.

Which progesterone is best for me?

If one Googles "natural progesterone cream" or "progesterone gel" there are dozens of products claiming to be the "best" and "authentic" natural

progesterone creams or gel. Just how does a woman determine which product is most suited to 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 and its equipment, processes, and packaging. PRO-FEME® natural progesterone creams are guaranteed stable, effective, and potent. 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 are 70% pure. 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 because cosmetic products do not require clinical trials to prove their worth.
 - 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 progesterone creams for women

available worldwide are **PRO-FEME®** 3.2% and 10% creams from Lawley Pharmaceuticals, Australia.

PRO-FEME® 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. Low progesterone in women is associated with PMS, miscarriage, breast changes, uterine changes, fatigue, lethargy, depression, irritability and mood changes. Applied topically to the skin, PRO-FEME® progesterone creams for women are the world's only clinically trialed and tested pharmaceutical grade progesterone creams using natural bio-identical progesterone. PRO-FEME® progesterone creams are listed with the Australian government (AUST L 95334 / L 70886).

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. As the principal of Lawley Pharmaceuticals, Mr. Buckley has presided over the development, research, clinical trial program, regulatory process, development and marketing of the company.

The Lawley Pharmaceuticals portfolio of products includes

Andro-Feme® 1% cream testosterone for women



Andromen® 2% and **Andromen®Forte 5%** testosterone creams for men



PRO-FEME® 3.2% and **10%** progesterone creams 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, hypogonadism, post natal 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. The effectiveness of transdermal progesterone cream on menopausal symptoms, lipids and bone markers
2. The effects of sequential transdermal progesterone cream on endometrium bleeding pattern and salivary levels in post-menopausal women
3. Evaluation of serum progesterone levels after topical applications of Andro-Feme® cream in post menopausal women with symptoms of progesterone deficiency
4. Systemic absorption after transdermal application of labeled progesterone in rats
5. Plasma and saliva concentrations of progesterone in pre- and post-menopausal women after topical application of progesterone cream
6. The effect of progesterone replacement therapy on sexuality, mood and cognition of post-menopausal women
7. Long-Term pharmacokinetics and clinical efficacy of Andromen®Forte 5% cream for androgen replacement in hypogonadal women.
8. Transdermal progesterone therapy improves well-being, mood, and sexual function in premenopausal women.
9. The pharmacokinetics of Andro-Feme®1% progesterone cream following two week, once daily application in progesterone deficient women.

Where can I find out more?

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Faculty: Nehmat Houssami, MBBS, MPH, MEd, FASBP, FAFPHM, PhD, Screening & Test Evaluation Program, School of Public Health, University of Sydney, Sydney, Australia and J. Michael Dixon, MBChB,MD, FRCS, FRCSEd, FRCP, Edinburgh Breast Unit, Western General Hospital, Edinburgh, Scotland. Originally published in Geriatrics & Aging, Volume 9, Number 9, October 2006, Pages 600-606.
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Glossary

You may hear these terms discussed in reference to yourself, your spouse, or your daughter:

Alfa-fetoprotein (AFP): A tumor marker for certain cancers of the ovaries and testes. Adults should have less than 15 nanograms of alfa-fetoprotein per milliliter of blood.

Amenorrhea: The monthly menstrual cycle ceases due to one of these causes:

- Menopause
- Pregnancy
- Exercising too much
- Not eating enough (anorexia nervosa)
- Extreme stress
- A serious underlying medical benign breast disease, such as uremia from end-stage renal disease (ESRD or kidney failure)

Anemia: Lack of blood, usually due to iron deficiency anemia. Anemic people feel tired and are withdrawn and pale. Dark skinned people have pale mucous membranes. Your family doctor orders a Complete Blood Count and ferritin levels to confirm that you have anemia, and will likely prescribe iron supplements.

β hCG: Pronounced Beta HCG. Pregnant women excrete this pregnancy hormone 10 days after conception. Males with carcinoma of the testicles excrete β hCG. If you had cancer surgery but are still excreting β hCG, then there is residual cancer that must be removed.

CA-15-3: Cancer Antigen 15-3, which is elevated in 3/4 of patients with metastatic breast cancer.

CA-125: Cancer Antigen 125 is a tumor marker for ovarian cancer.

CA-549: Cancer Antigen 549 is elevated in half of patients with advanced breast cancer.

Dysmenorrhea: Painful menstruation. If it is caused by excessive prostaglandins, dysmenorrhea can usually be relieved with ibuprofen (Motrin), massage, heat packs, adequate rest, and mild aerobic exercise, like walking. If it is caused by PCOS, hyperplasia, submucosal fibroids, or another uterine abnormality, the doctor must investigate further. Progesterone often relieves the pain associated with heavy menstruation from hyperplasia or fibroids.

Fibroid tumors: Benign (non-cancerous) uterine tumors that can cause pain and heavy bleeding.

Fibrosis: Scar tissue replaces healthy tissue as a result of degeneration, injury, or infection.

FNAC: Fine needle aspiration cytology.

FSH (follicular stimulating hormone): A hormone produced by the pituitary gland and the placenta, which stimulates the ovaries and controls reproduction.

Gonadotropin levels: The pituitary gland secretes a group of hormones called gonadotropins, which stimulate the testicles and ovaries. Girls with Turner syndrome possess at least one extra X chromosome(s), which usually causes their pituitary glands to produce too much of the gonadotropins FSH (follicular stimulating hormone) and LH (luteinizing hormone).

Hyalinized: Healthy tissue is replaced by hyaline (clear or translucent white, glassy collagen fibers) due to degeneration.

Hyperplasia: Overgrowth of tissue because of: Overstimulation by estrogen during perimenopause; estrogen-mimicking chemical toxins in the environment, such as pesticides on produce and phthalates in cosmetics and plastics; antibiotics and growth hormones in meat and milk; and obesity.

Hypothalamus: The section of the brain that regulates body temperature, chemical balance, the pituitary gland, and the autonomic nervous system. The hypothalamus is part of the limbic system, so it regulates sexual appetite, eating, sleep, and emotions. It influences heart and breathing rates and blood pressure. The hypothalamus is located in the grey matter, below the thalamus, in the center of the brain. The pituitary gland hangs on a stalk below the hypothalamus.

LH (luteinizing hormone): A gonadotropic hormone released by the pituitary gland in the brain, which stimulates females to ovulate (release an egg).

Lymphedema: Swollen lymph glands.

Mastectomy: Surgical removal of the breast.

Mammotone: A vacuum-assisted breast biopsy used to remove adenomas less than 3 cm in diameter. A radiologist performs an ultrasound or mammogram to help the surgeon find the adenosis. The small lump is sucked up through a needle.

Mondor's Disease: Superficial vein irritation, cording, and clotting (thrombophlebitis) that affects the breast, chest wall, arm, or penis. Can be caused by ill-fitting clothes.

Osteoporosis: Bones that are brittle and break easily due to lack of calcium and sex hormones.

Menorrhagia: Heavy bleeding more than 80 ml per cycle, or 16 soaked sanitary pads per cycle, leading to iron deficiency anemia.

Oligomenorrhea: Scanty uterine bleeding, with cycles greater than 35 days, so there are four to nine periods per year.

PCOS: Polycystic ovary syndrome. Painful, liquid-filled cysts on the ovaries that cause irregular menstruation, abnormal hair growth, skin tags, dark skin patches, insulin resistance, weight gain, infertility, and miscarriage. It may have a genetic component.

Pituitary gland: Connected to the hypothalamus, the pituitary controls growth hormone, prolactin for milk production, and follicle stimulating hormone (FSH) to stimulate ovaries and testes. The pituitary stimulates the adrenal glands and the thyroid.

Polymenorrhea: One menstrual period every 2-3 weeks; this is too frequent.

Prostaglandin: Chemicals that control the contractions of the uterus. Prostaglandin level is highest when your menstrual period begins. Too much prostaglandin contracts the uterine muscle so hard that the blood supply is cut off, the uterus is starved for oxygen, and pain results. Prostaglandins from the uterus can leak into the bloodstream and cause nausea, vomiting, diarrhea, and headache.

T3, T4, and TSH: A panel of blood tests used to evaluate the thyroid gland in the neck. Women with thyroid imbalance do not ovulate (release eggs for fertilization).

Virilize: Encourage formation of male secondary sexual characteristics, such as beard growth, voice deepening, and strong muscle growth.

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Enquiries should be addressed to:

Lawley Pharmaceuticals, 61 Walcott Street, Mt Lawley, 6050, WA Australia

This brochure is presented by

Lawley Pharmaceuticals

61 Walcott Street

Mt Lawley Western Australia 6050

T. +61 (0)8 9228 9033 or 1800 627 506

F. +61 (0)8 9228 9455

E. info@lawleypharm.com.au

W. www.lawleypharm.com.au

USA and Canada

Toll free phone: 1-800-961-7813

Toll free fax: 1-800-961-7650

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