Abnormal Uterine Bleeding

A Guide for Patients

PATIENT INFORMATION SERIES

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ABNORMAL UTERINE BLEEDING

A Guide for Patients Revised 2012

A glossary of italicized words is located at the end of this booklet.

INTRODUCTION

Menstruation is considered normal when uterine bleeding occurs every 21 to 35 days and is not excessive. The normal duration of menstrual bleeding is between two and seven days. Abnormal uterine bleeding occurs when either the frequency or quantity of uterine bleeding differs from that mentioned above or the woman has spotting or bleeding between her menstrual periods. Abnormal uterine bleeding may be caused by a variety of factors. The two most common causes are structural abnormalities of the reproductive system and ovulation disorders. Women who are post-menopausal should seek prompt care from a doctor for any bleeding, as the causes of bleeding and concerns are different from those in women of reproductive age.

NORMAL OVARIAN FUNCTION

In women of reproductive age, the ovary secretes estrogen and progesterone into the bloodstream. These two hormones prepare the endometrium (the lining of the uterus) for implantation of a fertilized egg. The pituitary gland, located at the base of the brain, influences ovarian hormone production and ovulation by secreting two hormones, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Following stimulation by FSH and LH, a follicle containing an immature egg begins to develop within the ovary. As the follicle enlarges, it secretes increasing amounts of estrogen. When a sufficient amount of estrogen is secreted, the pituitary gland releases a large amount of LH, which causes the follicle to release its egg (ovulation). If the egg does not become fertilized or does not implant in the endometrium, the secretion of estrogen and progesterone starts to decline approximately seven days after ovulation. With declining levels of estrogen and progesterone, the lining of the uterus is shed as the menstrual period (approximately 12-16 days after ovulation).

The cyclical release of FSH and LH from the pituitary gland is tightly regulated and easily disrupted. When the pituitary gland does not release appropriate quantities of FSH or LH, ovulation may not occur and the cycle may be disrupted. In some women who do not ovulate, the endometrium is stimulated by continuous exposure to estrogen without sufficient levels of progesterone to allow for complete shedding of the endometrial lining. This eventually may result in irregular or heavy bleeding. If estrogen exposure is continuous, cells within the endometrium also may become overstimulated and eventually develop into endometrial cancer.

CAUSES OF ABNORMAL UTERINE BLEEDING

Abnormal uterine bleeding (AUB) may be due to structural abnormalities of the uterus. Some of the more common structural causes of abnormal uterine bleeding include benign (non-cancerous) lesions of the uterus such as polyps, fibroids (myomas), and adenomyosis (uterine thickening caused by endometrial tissue moving into the outer walls of the uterus) (Figure 1). Other causes include bleeding associated with early pregnancy, including miscarriage and ectopic pregnancy, as well as bleeding disorders that affect the ability of the blood to clot normally. Lesions of the cervix or vagina (benign and cancerous), chronic infections of the endometrial lining (endometritis), scar tissue (adhesions) in the endometrium, and the use of an intrauterine device (IUD) also may be associated with abnormal uterine bleeding. Additional causes of abnormal bleeding include medications that can affect the normal release of estrogen and progesterone; chronic medical problems such as diabetes mellitus or disorders of the liver, kidney, thyroid gland, or adrenal glands; or other medical problems that can affect the production and metabolism of estrogen and progesterone. Emotional or physical stress as well as significant changes in body weight may disrupt the pituitary's release of FSH and LH and prevent ovulation.

Anovulatory or Dysfunctional Uterine Bleeding (DUB)

Dysfunctional uterine bleeding is the occurrence of uterine bleeding unrelated to structural abnormalities of the uterus or the endometrial lining. It is a diagnosis of exclusion made after structural causes of bleeding and chronic medical diseases have been ruled out. Other causes of abnormal bleeding must also be ruled out, including pregnancy complications and medications that influence hormonal action or affect clotting. Dysfunctional bleeding occurs more commonly in the first five years after a woman starts menstruating and as she approaches menopause, but it can occur at any time period. The cause of DUB is anovulation, the absence

of ovulation and the orderly secretion of estrogen and progesterone, and may alert the woman and her physician to the fact that she is no longer ovulating normally.

Figure 1

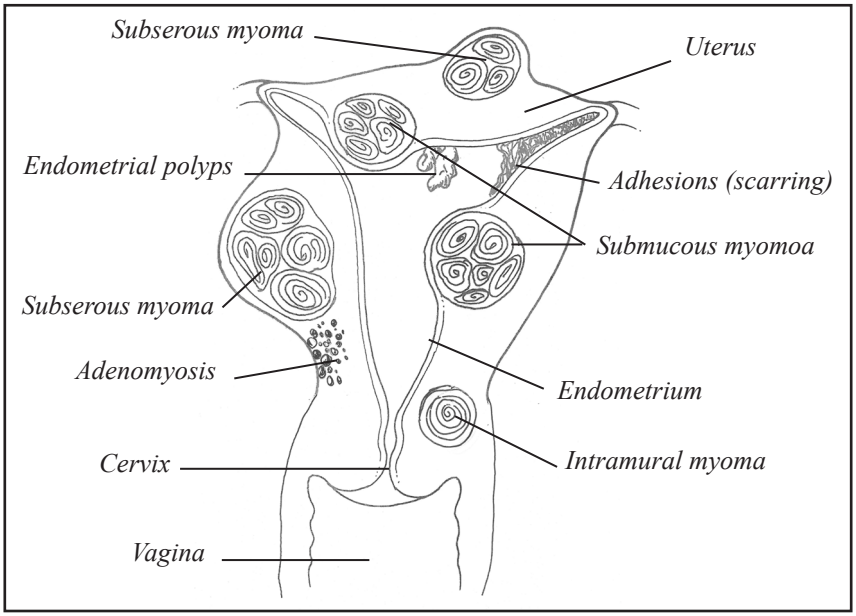

Figure 1. Causes of abnormal uterine bleeding.

DIAGNOSIS

Women who experience abnormal uterine bleeding should be evaluated by a physician. A medical history, discussion of possible contributing factors, and a detailed physical exam are indicated. A variety of diagnostic techniques are available for determining the cause of abnormal uterine bleeding.

Diagnostic Procedures

After performing a physical exam and ordering blood tests, a doctor may recommend an imaging study in order to better evaluate the appearance of the uterus, including the shape, size, and presence of any obvious structural abnormality. A variety of techniques are available to visualize the uterus and pelvic organs.

Ultrasound (sonogram) is a procedure which uses high-frequency sound waves to produce a picture of the pelvic structures. This is the most commonly used imaging method for the pelvic organs and does not

involve the use of radiation. The ultrasound is frequently performed both on top of the abdomen and pelvis as well as from within the vagina. A sonohysterogram may be performed in the office or in a radiology unit. During this procedure, a small catheter is first inserted into the cervix through which a sterile solution (such as saline or water) may be injected under ultrasound guidance. The water allows the doctor to see inside the uterine cavity to look for polyps, fibroids, or scar tissue. Abnormalities of the endometrium may also be detected by a hysterosalpingogram (HSG). This entails the slow injection of an iodine-containing solution into the uterine cavity under x-ray guidance so that the contours of the endometrium and fallopian tubes can be seen. Less commonly, computerized tomography (CT) and magnetic resonance imaging (MRI) can be used to depict a three-dimensional image of internal organs including the uterus. MRI is often more useful than CT in visualizing pelvic structures and may be particularly useful in patients where adenomyosis is suspected. The doctor may recommend an endometrial biopsy, an office procedure, to examine a sample of the uterine lining to rule out cancerous and noncancerous abnormalities.

Hysteroscopy is a useful procedure in which a thin telescope-like instrument is placed through the cervix into the uterus which allows visual inspection of the entire uterine cavity (Figure 2). It may allow the physician to identify specific areas of the endometrium that may be biopsied or removed with special instruments. Hysteroscopy may be performed under general anesthesia or as an office procedure. For more information on hysteroscopy, refer to the American Society for Reproductive Medicine (ASRM) patient information booklet titled, *Laparoscopy and Hysteroscopy*. In some circumstances, a dilation and curettage (D&C) may be recommended to further assess the endometrial tissue. This can be performed at the same time as hysteroscopy in many circumstances. D&C may also be recommended for control of persistent or heavy bleeding in women for whom other methods have been ineffective. Generally, however, hysteroscopy is performed at the same time as the D&C, and D&C is only effective in treating abnormal bleeding in that particular menstrual cycle.

Figure 2

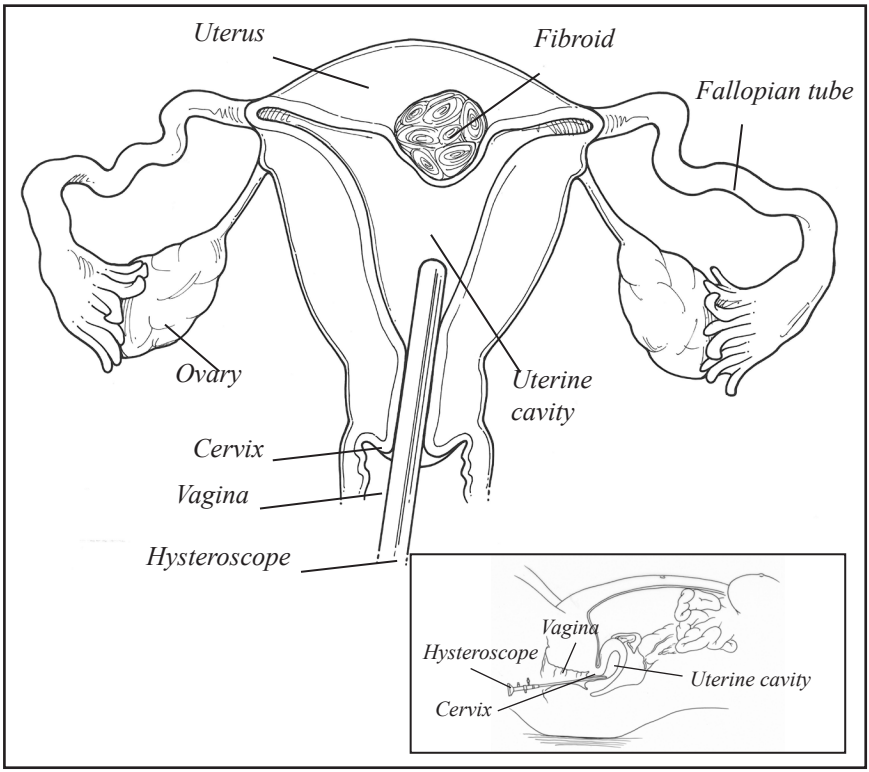

Figure 2. Frontal view of hysteroscopy. See inset for side view.

Laboratory Studies

Laboratory studies also aid in diagnosing abnormal uterine bleeding. A pregnancy test is always performed because abnormal bleeding in the reproductive years is commonly due to abnormalities associated with pregnancy. Often a blood test will be obtained to check for anemia (low blood count) or a blood clotting disorder. When structural disturbances of the reproductive tract have been ruled out, a blood test to measure pituitary hormones, such as prolactin, FSH, and thyroid hormones, may be performed. If there is evidence of abnormal hair growth on the face or down the middle of the body, the cause may be polycystic ovary syndrome (PCOS). PCOS often is associated with irregular or heavy menstruation. For more information on PCOS, refer to the ASRM patient information booklet titled *Hirsutism and Polycystic Ovary Syndrome*. Increased body hair may lead the physician to measure the androgens (hormones)

testosterone and dehydroepiandrosterone sulfate (DHEAS). Additional tests of the liver, kidney, pancreas, and other major organs may be useful, depending upon each woman's medical history. Laboratory studies for abnormal uterine bleeding will be based on the physician's clinical judgment as to the underlying cause of the bleeding.

TREATMENT

The individual therapy recommended to you by your doctor will be tailored to the specific cause of abnormal bleeding. Structural abnormalities of the reproductive tract such as fibroids, polyps, or scar tissue often can be treated during hysteroscopy. Surgical instruments can be inserted through the hysteroscope to remove or correct structural abnormalities within the uterine cavity. Generally, patients can return to normal activities within 24 hours after hysteroscopy. Serious complications are rare.

Women who have adequate levels of estrogen but who do not ovulate can be effectively treated with synthetic progestins such as medroxyprogesterone acetate using dosages of 5 to 10 mg each day orally for more than 10 days. Other progestins, including natural progesterone, are available as oral capsules, vaginal suppositories, or intramuscular injections and also are effective in promoting complete shedding of the endometrial lining. In many instances, patients can be treated with low-dose combination oral contraceptives (OCs), which provide both estrogen and progestins and promote regular menstruation. This may be a particularly useful choice for individuals who also desire birth control.

Menorrhagia

For women with menorrhagia (excessively prolonged or heavy menstruation), the administration of an estrogen may be recommended to temporarily stop the bleeding and stabilize the endometrial lining. Often the physician will recommend an endometrial biopsy under such circumstances. Estrogens can be administered orally, such as conjugated estrogens, using dosages of 1.25 to 5 mg every six hours for a 12- to 24-hour period. Alternatively, intravenous estrogens at dosages of 20 to 25 mg can be administered every four to six hours to control heavy bleeding. After several days of estrogen therapy, progestins should be administered orally for 12 days to try to achieve a controlled bleeding episode.

Heavy uterine bleeding may be controlled with the use of low-dose OCs. A combination OC formulation may be administered as two to four tablets

per day for up to seven days to control severe menorrhagia. Thereafter, an interruption of OC use for five to seven days may be recommended, and a controlled withdrawal flow generally follows. Subsequently, low dose OCs may be used in a standard fashion to facilitate orderly menstrual bleeding. If OC therapy is used in women over the age of 40, reproductive tract abnormalities, malignancies, and medical conditions which may prevent the use of these medications should first be excluded. For more information on the use of OCs to control bleeding, refer to the ASRM patient fact sheet titled *Noncontraceptive Benefits of Birth Control Pills*.

Tranexamic acid can be used for heavy bleeding episodes. This orally administered medication is used twice per day and has been shown to cause a major reduction in menstrual blood flow.

Levonorgestrel-containing IUDs are useful in treating DUB heavy menstrual bleeding and may be the most effective therapy. Prostaglandin synthesis inhibitors, including ibuprofen and related compounds, also have been shown to reduce excessive menstrual bleeding in some women. This may be useful particularly in women with menorrhagia following the insertion of an IUD.

Occasionally, the physician may recommend the use of gonadotropin-releasing hormone (GnRH) analogs to temporarily control excessive uterine bleeding, particularly for the treatment of severe menorrhagia, which may cause anemia. These compounds temporarily stop the release of FSH and LH from the pituitary gland and cause ovarian estrogen production to fall to menopausal levels. Short-term use of GnRH analogs in combination with iron supplementation may improve or correct the anemia.

Surgical approaches include removal of any uterine abnormalities with the use of the hysteroscope. Surgical removal of fibroids (myomectomy) may be recommended for women with menorrhagia who fail to respond to hormonal therapy. The type of surgical technique will depend upon both the size and location of the fibroids. Myomectomy may be performed through hysteroscopy, laparoscopy (traditional or robotic), and by an abdominal incision (laparotomy). Some women may choose to have their uterus removed (hysterectomy) by one of several different routes (vaginal, laparoscopy, laparotomy). For more information on fibroids, refer to the ASRM patient information factsheet *Treatment of Uterine Fibroids*.

Additionally, endometrial ablation may be recommended for women who no longer desire fertility. This procedure, which is performed under general anesthesia, uses thermal radiofrequency, cryosurgery (freezing), or a laser beam to remove the endometrial lining and generally corrects heavy menstrual flow. It is important to exclude serious endometrial lesions prior to performing this procedure. Although the goal is to stop menstrual bleeding completely, most often menstrual periods simply become lighter following this procedure. Ablation should not be performed if a woman still desires future fertility. For more information on endometrial ablation, refer to the ASRM patient information factsheet *Endometrial Ablation*.

Only rarely will a hysterectomy be recommended for heavy menstrual bleeding. This only should be considered for patients who no longer desire childbearing and who have failed other hormonal and/or surgical treatments and who have been thoroughly evaluated.

Pituitary and Glandular Dysfunction

Disorders of the pituitary and thyroid glands can cause anovulation and menstrual irregularity. Individuals with inadequate production of thyroid hormone (hypothyroidism) can be treated with daily oral replacement of thyroid hormone. Excess thyroid hormone production (hyperthyroidism) may be treated with oral medications, radioactive iodine, or surgical removal of all or part of the thyroid gland. The treatment of hyperprolactinemia (excessive release of prolactin from the pituitary) is generally treated with the oral medication cabergoline or bromocriptine. Individuals with elevated levels of prolactin may be advised to have an imaging study, such as a CT scan or MRI, of the pituitary gland to determine if there is evidence of a pituitary lesion. Pituitary adenomas are the most common benign tumors of the pituitary gland and are often associated with excessive release of prolactin. If pituitary adenomas are large, they may be treated surgically. Sometimes changes in exercise and/or dietary habits (to reduced calorie intake or a vegetarian diet) can cause changes in many of these hormones and lead to irregular bleeding. Such lifestyle changes cause FSH and LH to be very low or close to undetectable and this may suggest a proper evaluation. An elevated FSH level may indicate impending ovarian failure, either due to menopause or to early menopause, also known as premature ovarian failure (POF). For more information on POF, refer to the ASRM patient information factsheet titled *Premature Ovarian Failure.*

Polycystic Ovary Syndrome (PCOS)

Patients with PCOS must have their therapy individualized depending upon whether their goal is restoration of fertility or regular menstruation. For individuals with irregular uterine bleeding who are not currently attempting to get pregnant, intermittent progestin therapy (medroxyprogesterone acetate 5 to 10 mg orally for 12 to 14 days a month) or oral contraceptives may be recommended to establish regular bleeding episodes and to reduce the risk of hyperplasia and cancer. Estrogen and progestin together, as in OCs, may be more effective than progestin therapy alone. Women with PCOS who are attempting to get pregnant are generally treated with clomiphene citrate. If clomiphene is ineffective, alternative treatment programs can be recommended. PCOS can be associated with high blood pressure, heart disease, acne, excess body hair (hirsutism), obesity, and diabetes mellitus, so proper medical attention and treatment are important. For further information on PCOS and fertility treatment for patients with PCOS, refer to the ASRM patient information booklets and fact sheets on PCOS and hirsutism.

SUMMARY

Abnormal uterine bleeding is a common problem in women of reproductive age that usually can be corrected with surgery or medication. Surgery may be able to correct structural causes of abnormal bleeding. If there are no structural causes, medical therapy often can restore regular menstrual cycles. Whatever the cause of abnormal uterine bleeding, the many treatments available today usually can resolve the problem. Patients should speak to their doctors about which medical or surgical options may be best for them.

GLOSSARY

Adenoma. A benign (non-cancerous) growth of cells that usually does not invade adjacent tissue. A pituitary adenoma can disrupt ovulation and menstruation and often is associated with excessive prolactin production.

Adenomyosis. A benign (non-cancerous) invasion of endometrial tissue into the muscular wall (myometrium) of the uterus; is associated with painful or heavy menstrual periods.

Adhesions (scar tissue). Bands of fibrous scar tissue that may bind the pelvic organs and/or loops of bowel together. Adhesions can result from previous infections, endometriosis, or previous surgeries.

Adrenal glands. Glands located above each kidney that secrete a large variety of hormones (cortisol, adrenaline, and others) that help the body withstand stress and regulate metabolism. Altered function of these glands can disrupt menstruation, cause inappropriate hair growth, and affect blood pressure.

Androgen. In men, androgens are the "male" hormones produced by the testes which are responsible for encouraging masculine characteristics. In women, androgens are produced in small amounts by both the adrenal glands and ovaries. In women, excess amounts of androgens can lead to irregular menstrual periods, obesity, excessive growth of body hair (hirsutism), and infertility.

Anemia. A reduction in the number of red blood cells, which carry oxygen in the body. Anemia is characterized by weakness or listlessness. It can be a consequence of abnormal bleeding.

Anovulation. Absent ovulation. Failure of the ovary to ovulate regularly.

Bromocriptine. A drug used to suppress the production of prolactin by the pituitary gland. The brand name is Parlodel®.

Cervix. The lower, narrow end of the uterus that connects the uterine cavity to the vagina.

Clomiphene citrate. An oral anti-estrogen drug used to induce ovulation in the female. It also sometimes is used to increase testosterone levels in the infertile male, which may, in turn, improve sperm production. The brand names are Clomid ® and Serophene®.

Computerized tomography (CT). An x-ray imaging technique that creates a three-dimensional image of internal organs.

Diabetes mellitus. A condition due to abnormal production of insulin resulting in abnormally elevated blood glucose (sugar) levels.

Dilation and curettage (D&C). An outpatient surgical procedure during which the cervix is dilated and the lining of the uterus is scraped out.

The tissue often is used for microscopic examination for the presence of abnormality or pregnancy tissue.

Dysfunctional uterine bleeding (DUB). Abnormal uterine bleeding with no evidence of mechanical or structural cause. The most common cause of DUB is deficient or excessive production of estrogen and/or progesterone.

Ectopic pregnancy. A pregnancy that implants outside of the uterus, usually in the fallopian tube. The tube may rupture or bleed as the pregnancy grows and create or result in a serious medical situation.

Endometrial ablation. A hysteroscopic or non-hysteroscopic procedure used to remove, burn, or freeze most of the endometrium (uterine lining); sometimes used to treat abnormal uterine bleeding.

Endometrial biopsy. Removal of a small piece of tissue from the endometrium (lining of the uterus) for microscopic examination. The results may indicate whether or not the endometrium is at the appropriate stage for successful implantation of a fertilized egg (embryo) and/or if it is inflamed or diseased.

Endometritis. An inflammation of the endometrium caused by bacterial invasion.

Endometrium. The lining of the uterus that is shed each month as the menstrual period. As the monthly cycle progresses, the endometrium thickens and thus provides a nourishing site for the implantation of a fertilized egg.

Estrogens. The female sex hormones produced by the ovaries that are responsible for the development of female sex characteristics. Estrogens largely are responsible for stimulating the uterine lining to thicken during the first half of the menstrual cycle in preparation for ovulation and possible pregnancy. They also are important for healthy bones and overall health. A small amount of these hormones also is produced in the male when testosterone is converted to estrogen.

Fallopian tubes. A pair of hollow tubes attached one on each side of the uterus through which the egg travels from the ovary to the uterus. Fertilization usually occurs in the fallopian tube. The fallopian tube is the most common site of ectopic pregnancy.

Fibroids. Benign (non-cancerous) tumors of the uterine muscle wall that can cause abnormal uterine bleeding. Also known as leiomyomas or myomas.

Follicle. A fluid-filled sac located just beneath the surface of the ovary that contains an egg (oocyte) and cells that produce hormones. The

follicle increases in size and volume during the first half of the menstrual cycle. At ovulation, the follicle matures and ruptures, releasing the egg. As the follicle matures, it can be visualized by ultrasound.

Follicle-stimulating hormone (FSH). In women, FSH is the pituitary hormone responsible for stimulating follicular cells in the ovary to grow, stimulating egg development, and the production of the female hormone estrogen. In the male, FSH is the pituitary hormone that travels through the bloodstream to the testes and helps stimulate them to manufacture sperm.

GnRH analog. A long-acting drug that blocks the release of hormones, stops ovulation, and decreases the body's production of estrogen. Prolonged use of GnRH analogs causes decreased hormone production and menopausal levels of estrogen. The brand names are Lupron®, Depo Lupron®, Synarel®, and Zoladex®.

Hysterectomy. The surgical removal of the uterus. Hysterectomy may be performed through an abdominal incision (laparotomy), through the vagina (vaginal hysterectomy), through laparoscopy or robotic assisted laparoscopy, or by laparoscopic assisted vaginal hysterectomy (LAVH). Sometimes the ovaries and fallopian tubes also are removed.

Hysterosalpingogram (HSG). An x-ray procedure in which a special iodine-containing dye is injected through the cervix into the uterine cavity to illustrate the inner shape of the uterus and degree of openness (patency) of the fallopian tubes.

Hysteroscope. A thin, lighted telescope-like instrument that is inserted through the vagina and cervix into the uterine cavity to allow viewing of the inside of the uterus.

Hysteroscopy. The insertion of a long, thin, lighted telescope-like instrument, called a hysteroscope, through the cervix and into the uterus to examine the inside of the uterus. Hysteroscopy can be used to both diagnose and surgically treat uterine conditions.

Intrauterine device (IUD). A contraceptive device placed within the uterus; also may be used to prevent scar tissue formation following uterine surgery.

Laparotomy. Major abdominal surgery through an incision in the abdominal wall.

Lesions. Growths or abnormalities of normal anatomy. Examples include scar tissue, polyps, and uterine fibroids.

Luteinizing hormone (LH). In women, the pituitary hormone that triggers ovulation and stimulates the corpus luteum of the ovary to

secrete progesterone and other hormones during the second half of the menstrual cycle. In men, LH is the pituitary hormone that stimulates the testes to produce the male hormone testosterone.

Magnetic resonance imaging (MRI). A diagnostic procedure that absorbs energy from specific high-frequency radio waves. The picture produced by measurement of these waves can be used to form precise images of internal organs without the use of x-ray techniques. No radiation exposure occurs.

Menopause. Cessation of ovarian function and menstruation that usually occurs naturally but also can be a result of surgery. Menopause can occur between the ages of 42 and 56 but usually occurs around the age of 51, when the ovaries stop producing eggs and estrogen levels decline.

Menorrhagia. Regular but heavy menstrual bleeding which is excessive in either amount (greater than 80 cc – approximately five tablespoons) or duration (greater than seven days).

Myomas. Benign (non-cancerous) tumors of the uterine muscle wall that can cause abnormal uterine bleeding and miscarriage. Also see fibroids.

Myomectomy. The surgical removal of myomas (fibroids) from the uterus.

Ovaries. The two female sex glands in the pelvis, located one on each side of the uterus. The ovaries produce eggs and hormones including estrogen, progesterone, and androgens.

Ovulation. The release of a mature egg from its developing follicle in the outer layer of the ovary. This usually occurs approximately 14 days before the next menstrual period (the 14th day of a 28-day cycle).

Pituitary gland. A small hormone-producing gland located just beneath the hypothalamus in the brain which controls the ovaries, thyroid, and adrenal glands. Ovarian function is controlled through the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Disorders of this gland may lead to irregular or absent ovulation in the female and abnormal or absent sperm production in the male.

Polycystic ovary syndrome (PCOS). A condition in which the ovaries contain many follicles that are associated with chronic anovulation and overproduction of androgens (male hormones). The cystic follicles exist presumably because the eggs are not expelled at the time of ovulation. Symptoms may include irregular menstrual periods, obesity, excessive growth of central body hair (hirsutism), and infertility. PCOS can also be associated with heart disease, hypertension, or diabetes. Also called Stein-Leventhal syndrome.

Polyps. A general term that describes any mass of tissue which bulges or projects outward or upward from the normal surface level.
Progesterone. A female hormone usually secreted by the corpus luteum after ovulation during the second half of the menstrual cycle (luteal phase). It prepares the lining of the uterus (endometrium) for implantation of a fertilized egg and also allows for complete shedding of the endometrium at the time of menstruation. In the event of pregnancy, the progesterone level remains stable beginning a week or so after conception.
Progestins. A synthetic hormone that has an action similar to progesterone. Synonymous with progestational hormones.
Prolactin. A hormone normally secreted by the pituitary gland into the bloodstream for the purpose of maintaining milk production during lactation. When secreted in excessive amounts, it may lead to irregular or absent menstrual periods and may produce a milk-like discharge from the breasts.
Thyroid gland. A large, two-lobed, endocrine gland located in front of and on either side of the trachea (windpipe) in the neck that secretes the hormone thyroxin into the bloodstream. Thyroxin maintains normal body growth and metabolism.
Ultrasound (sonogram). A picture of internal organs produced by high frequency sound waves viewed as an image on a video screen; used to monitor growth of ovarian follicles or a fetus and to retrieve eggs. Ultrasound can be either performed abdominally or vaginally.
Uterus (womb). The hollow, muscular female reproductive organ in the pelvis where an embryo implants and grows during pregnancy. The lining of the uterus, called the endometrium, produces the monthly menstrual blood flow when there is no pregnancy.

For more information on this and other reproductive health topics visit www.ReproductiveFacts.org

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Notes

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