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Medications for Inducing Ovulation

A Guide for Patients

PATIENT INFORMATION SERIES

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Medications for Inducing Ovulation

A Guide for Patients Revised 2012

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

INTRODUCTION

Approximately 25% of infertile women have problems with ovulation. These include the inability to produce fully matured eggs or failure to "ovulate" (release) an egg. The inability to produce and/or release eggs is called anovulation. Fertility specialists use a group of medications, often called "fertility drugs," to temporarily correct ovulatory problems and increase a woman's chance for pregnancy. Fertility drugs may be used to correct other fertility problems such as improving the lining of the *uterus* (endometrium) in addition to inducing ovulation. In certain circumstances, these medications also may be used to stimulate the development of multiple eggs, such as in an *in vitro fertilization (IVF)* cycle. This booklet explains the basics of normal ovulation and the diagnosis and treatment of ovulatory problems. The specific uses for several types of ovulation drugs are presented, along with the intended results and possible side effects of each drug.

Normal Reproductive Anatomy

The ovaries are two small glands, each about 1½ inches long and 3/4 of an inch wide, located in a woman's pelvic cavity (Figure 1). They are attached to ligaments and located on both sides of the uterus (womb), usually below the *fallopian tubes.* About once a month, an egg matures in a follicle (a fluid-filled ovarian cyst containing the egg) after which it is released by one of the ovaries. The *fimbriae* (finger-like projections) of the fallopian tubes sweep over the ovary and move the egg into the tube. If sperm are present in the woman's reproductive tract, the egg may be fertilized in the tube. The fertilized egg (now called an embryo) begins to divide. The embryo travels through the tube and into the uterus where it implants in the endometrium (uterine lining). The embryo's journey through the tube takes four to five days.

Figure 1

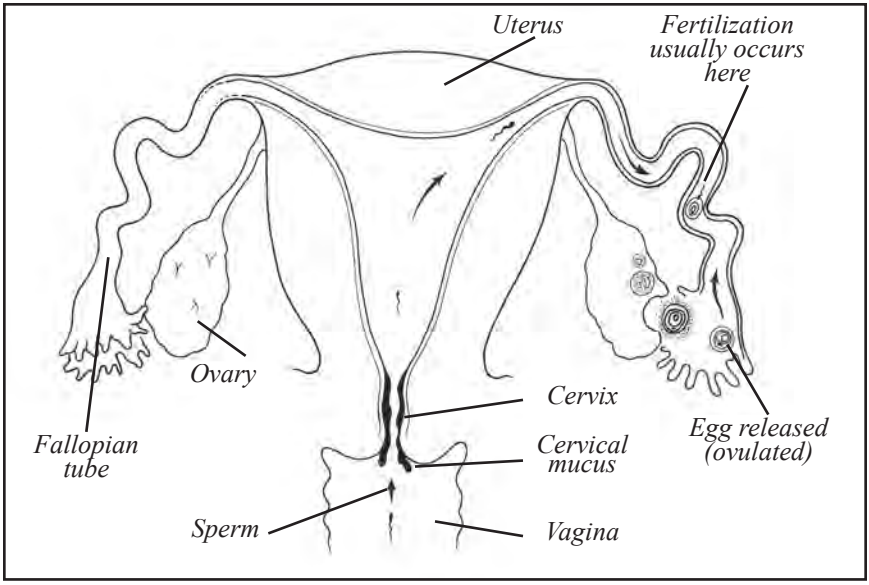

Figure 1. Diagram showing ovulation. Fertilization usually occurs in the fallopian tube.

THE MENSTRUAL CYCLE

The menstrual cycle is divided into three phases: the follicular phase, the ovulatory phase, and the *luteal phase* (Figure 2).

The Follicular Phase

The follicular phase lasts about 10 to 14 days, beginning with the first day of menstruation and lasting until the *luteinizing hormone (LH)* surge. During the follicular phase, the hypothalamus, located just above the *pituitary gland* in the brain, releases *gonadotropin-releasing hormone (GnRH)*. This hormone directs the pituitary gland to release *follicle-stimulating hormone (FSH)*. FSH stimulates the development of *follicles* in the ovaries containing eggs. Ordinarily, one of these follicles will become the dominant follicle, and its egg will reach full maturity. The other follicles that were stimulated stop developing, and their eggs degenerate through a process called atresia. The dominant follicle increases in size and secretes estrogen into the bloodstream. The rising levels of estrogen cause the pituitary to slow down the production of FSH.

The Ovulatory Phase

The ovulatory phase begins with the LH surge and ends with ovulation, which is the release of the egg from the dominant ovarian follicle. As

ovulation approaches, estrogen levels rise and trigger the pituitary gland to release a surge of LH. About 32 to 36 hours after the onset of this LH surge, the dominant follicle releases (ovulates) its egg.

The Luteal Phase

The luteal phase begins after ovulation and generally lasts about 12 to 16 days. After the egg is ovulated, the empty follicle that contained the egg becomes known as the *corpus luteum*. The corpus luteum secretes *progesterone*, a hormone that helps prepare the endometrium for implantation of the *embryo* and pregnancy. If the egg is fertilized by a sperm, the resulting embryo reaches the uterus several days later and begins to implant in the *endometrium*. If an embryo does not implant, progesterone levels decline. The endometrium then breaks down, is shed in the process of menstruation, and the cycle begins again. Even though your cycles may continue to be regular in your 30s and 40s, the eggs that ovulate each month tend to be of poorer quality than those from your 20s. During this time in your life, your physician may wish to evaluate your *ovarian reserve*, which will help you understand your potential ability to get pregnant, based on the number and quality of eggs remaining in your ovaries.

Figure 2

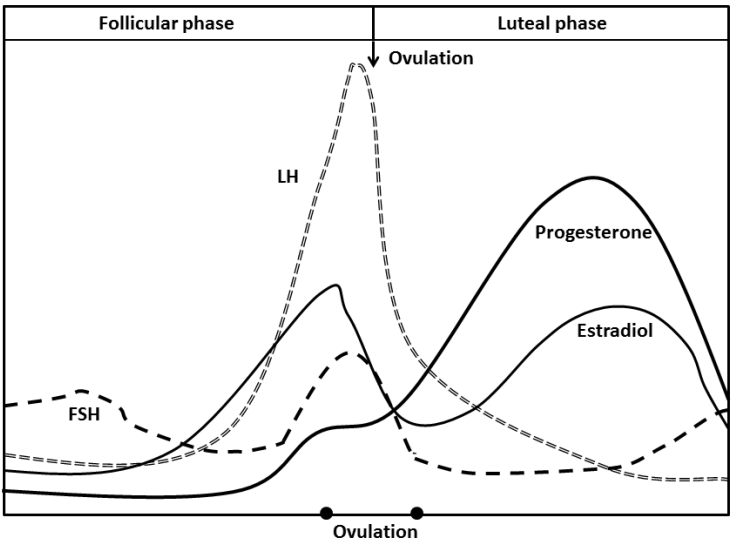

Figure 2. Hormonal cycle in women with normal ovulation. The follicular phase is the phase in which the follicle is growing and secreting estrogen. The ovulatory phase is the 48-hour period characterized by the LH surge and the release of the egg (ovulation). The luteal phase is characterized by secretion of large amounts of progesterone and estrogen.

DIAGNOSIS

Ovulation can be detected and confirmed in several ways. A woman who menstruates consistently each month probably is also ovulating each month, with ovulation occurring about 14 days before the first day of each menstrual period. However, it is important to remember that a woman can have uterine bleeding even though she never ovulates. There are several ways to detect ovulation, including commercially available ovulation prediction kits that measure LH and basal body temperature (BBT) charts. Other diagnostic tests used to detect ovulation include measuring luteal phase serum progesterone levels, monitoring ovarian follicles with serial transvaginal ultrasounds, and endometrial biopsies.

TREATMENT: OVULATION MEDICATION

Who Needs Ovulation Medication?

Medications for inducing ovulation are used to treat women who ovulate irregularly. Women with irregular menstrual cycles *(oligo-ovulatory)* or absence of menstruation (amenorrhea) are likely to have ovulatory dysfunction. Prior to the administration of fertility drugs to induce ovulation, a diagnostic evaluation should be performed to try to determine the cause of ovulatory dysfunction. Women might not ovulate because of polycystic ovary syndrome (PCOS), insufficient production of LH and FSH by the pituitary, ovaries that do not respond well to normal levels of LH and FSH, thyroid disease, prolactin excess, obesity, eating disorders, or extreme weight loss or exercise. Sometimes the cause of anovulation cannot be identified confidently. Women with ovulatory dysfunction are the subgroup of infertile patients that is most likely to benefit from ovulation induction with fertility drugs. *Clomiphene citrate* is the most frequently used oral medication to stimulate ovulation in these patients with ovulatory dysfunction.

Ovulation induction with fertility drugs is also commonly used in patients without ovulatory dysfunction to stimulate the ovaries to produce more than one mature follicle per cycle, leading to the release of multiple eggs. This controlled ovarian stimulation (COS), or *superovulation*, may be accomplished with either oral or injectable fertility medications. Superovulation, combined with either intercourse or intrauterine

insemination (IUI), is an empiric strategy for the treatment of several forms of infertility. The intent is to develop several mature eggs in hopes that at least one egg will be fertilized and result in pregnancy. Controlled ovarian stimulation is also an important component of IVF treatment. Prior to ovulation induction with fertility drugs, it is recommended that a patient's fallopian tube patency be confirmed by *hysterosalpingogram* (injection of a dye into the fallopian tubes) or *laparoscopy*. Patients with blocked fallopian tubes will not become pregnant with fertility drugs and should not undergo ovulation induction unless the purpose of the ovulation induction is to stimulate the ovaries in preparation for IVF. Also the male partner should have a semen analysis to help guide whether ovulation induction should be combined with intercourse, IUI, or IVF. For more information on IVF, consult the ASRM patient information booklet titled, *Assisted Reproductive Technologies*.

COMMONLY PRESCRIBED MEDICATIONS

The most commonly prescribed ovulation drugs are clomiphene citrate, FSH, human chorionic gonadotropin (hCG), and *human menopausal gonadotropin (hMG)*. Bromocriptine, *cabergoline*, GnRH, GnRH analogs, insulin-sensitizing agents, and LH have very specialized applications that are described after Table 1, which provides a summary of common ovulation drugs and their side effects (next page).

Table 1.Ovulation drugs and their most common side effects

Generic Name	Brand Name(s) (not all inclusive)	Form	Most Common Side Effects
Clomiphene Citrate	*Clomid®* *Serophene®*	*Tablets*	*• increased incidence of multiple births* *• thick, dry cervical mucus* *• occasional headaches or blurred vision* *• depression, mood swings* *• ovarian cysts, pelvic discomfort*
Metformin	*Glucophage®* *Fortamet®* *Riomet®* *Glumetza®*	*Tablets*	*• gastrointestinal* *• lactic acidosis* *• liver dysfunction*
Follicle Stimulating Hormone (FSH)	*Urinary derived:* *Bravelle®* *Recombinant DNA technology:* *Follistim®* *(follitropin beta)* *Gonal-F®* *(follitropin alpha)*	*Injection*	*• increased incidence of multiple births* *• increased incidence of miscarriage and premature delivery* *• breast tenderness, swelling, or rash at injection site* *• mood swings, depression* *• moderate to severe hyperstimulation syndrome (enlarged ovaries, abdominal pain, and bloating)*
Luteinizing Hormone (LH)	*Recombinant DNA technology:* *Luveris®* *(lutropin alpha)*	*Injection*	*• same as for FSH*
Human Chorionic Gonadotropin (hCG)	*Urinary derived:* *A.P.L.®* *Pregnyl®* *Novarel®* *Recombinant DNA technology:* *Ovidrel®* *(choriogonadotropin alpha)*	*Injection*	*• no known side effects if only taking hCG*
Human Menopausal Gonadotropin (hMG)	*Urinary derived:* *Repronex®* *Menopur®*	*Injection*	*• same as for FSH*

(Table 1 continued)

Generic Name	Brand Name(s) (not all inclusive)	Form	Most Common Side Effects
Dopamine agonists	*Parlodel® (bromocriptine)* *Dostinex® (cabergoline)*	*Tablet*	*• nausea, vomiting, nasal congestion* *• headache, dizziness, fainting* *• decreased blood pressure*
Gonadotropin-releasing Hormone (GnRH)	*Factrel®* *Lutrepulse®*	*Injection*	*• slight chance of multiple births* *• mild hyperstimulation syndrome* *• headache* *• nausea*
GnRH Agonists	*Lupron Depot® (Leuprolide Acetate)* *Lupron® (Leuprolide)* *Synarel® (Nafarelin Acetate)* *Zoladex® (Goserelin Acetate)*	*Injection* *Nasal spray* *Injectable implant*	*• hot flashes, headache* *• mood swings, insomnia* *• vaginal dryness* *• decreased breast size* *• painful intercourse* *• bone loss* *• symptoms occur in long-term use*
GnRH Antagonists	*Ganirelix Acetate®* *Antagon ® (ganirelix)* *Cetrotide® (cetrorelix acetate)*	*Injection*	*• same as GnRH agonists*
Aromatase Inhibitors- not FDA approved for this use	*Femara® (letrozole)* *Arimidex® (anastrazole)*	*Tablet*	*• may have similar effects as GnRH agonists during short term use for ovalation induction cycles* *• may increase the risk of birth defects*

Clomiphene Citrate

The most commonly prescribed ovulation drug is clomiphene citrate (for brevity, this booklet will refer to clomiphene citrate as "CC" or "clomiphene"). This drug is most often used to stimulate ovulation in women who have infrequent or absent ovulation. It is also used in combination with IUI as an empiric treatment for unexplained infertility, and sometimes in those who are unable to pursue more aggressive therapies involving greater costs, risk, or logistical demands.

The standard dosage is 50 -100 milligrams (mg) of clomiphene per day for five consecutive days. Treatment begins early in the cycle, usually on the third to fifth day after menstruation begins. If a woman does not have periods, a period can be induced by administering oral *progestin* for 10 days.

Clomiphene works by causing the pituitary gland to secrete more FSH. The higher level of FSH stimulates the development of ovarian follicles that contain eggs. As the follicles grow, they secrete *estrogen* into the bloodstream. If treatment is successful, about a week after the last tablet of CC is taken, the pituitary is hypersensitive to GnRH and releases an *LH surge*. The LH surge causes the egg to be released from the mature follicle during ovulation. It is important to determine whether a given dosage of clomiphene results in ovulation. Most doctors rely on the menstrual pattern, ovulation prediction kits, measurement of serum progesterone levels or the basal body temperature chart to monitor a patient's response to the standard dose of clomiphene.

A basal body temperature chart is a chart in which the patient's temperature is taken upon awakening using a special thermometer, and this temperature is plotted every morning before she gets up. The readings help identify ovulation, which is indicated by a persistent temperature rise of one-half degree or more. If there is doubt, however, measuring the progesterone level about 14 to 18 days after the start of clomiphene, or examining the ovaries with *ultrasound*, can help to determine if and when ovulation occurred.

If ovulation does not occur at the 50-mg dosage, CC may be increased by 50-mg increments in subsequent cycles until ovulation is achieved. Exceeding a dosage of 200 mg each day for five days is rarely of any benefit, and patients who fail to ovulate on a clomiphene dosage of 200 mg are likely to benefit from a different ovulation induction regimen such as injections of gonadotropins. Your physician will determine the appropriate dose for you. Occasionally, the physician may choose to add other medications to clomiphene if the drug is not successful in inducing ovulation. For more information about basal body temperature charts and ovulation detection, refer to the ASRM Patient Fact Sheet titled, *Ovulation Detection.*

The cervical mucus acts as a barrier to sperm. The properties of the cervical mucus may be altered in patients taking clomiphene citrate. Intrauterine

insemination frequently is used in conjunction with clomiphene ovulation induction by CC. Clomiphene sometimes can alter endometrial thickness, making it thin and unreceptive to implantation. The lowest dose of clomiphene sufficient to induce ovulation in anovulatory women is usually prescribed for at least three cycles to provide an adequate trial for most patients. Clomiphene will induce ovulation in about 80% of properly selected patients. Most authorities suggest that clomiphene be given for no more than six cycles, because the chance of pregnancy is very low after six cycles. After that, alternatives may be considered.

Women who have irregular/absent ovulation due to hypothalamic disorders or very low estrogen levels generally do not respond well to clomiphene. Women who are obese may have better success after weight loss. Clomiphene is generally tolerated well. Side effects are relatively common, but generally mild. Hot flashes occur in about 10% of women taking clomiphene, and typically disappear soon after treatment ends. Mood swings, breast tenderness, and nausea are also common. Severe headaches or visual problems, such as blurred or double vision, are uncommon, and virtually always reversible. If these side effects occur, it is prudent to stop treatment immediately and call the physician. Women who conceive with clomiphene have approximately a 10% chance of having twins. Triplet and higher order pregnancies are rare (<1%), but may occur. Ovarian cysts, which can cause pelvic discomfort, may form as a result of ovarian overstimulation. A pelvic exam or ultrasound may be performed to look for ovarian cysts before beginning another clomiphene treatment cycle. Side effects are more frequent with higher doses.

Aromatase Inhibitors

Aromatase inhibitors are medications that reduce estrogen levels. Although these medications are currently FDA approved for postmenopausal breast cancer, two drugs, letrozole and anastrozole, have been used successfully for ovulation induction. Typically, the pills are prescribed for five days starting on cycle day three, four or five. Studies indicate that pregnancy rates are comparable to clomiphene citrate. The manufacturer of letrozole recently listed premenopausal endocrine status as a contraindication to its use. Recent data have raised concern that letrozole may be associated with an increased risk of congenital abnormalities, although subsequent studies to date have not reproduced these findings.

Insulin-s Sensitizing Drugs

Insulin resistance and hyperinsulinemia are seen commonly in women with *polycystic ovary syndrome (PCOS)*. Although most women with PCOS will ovulate with clomiphene, many are resistant, and ultimately require an alternate treatment. When used alone for four to six months, insulin sensitizing agents such as metformin can restore cyclic ovulation and menses in some women with PCOS, although they are not currently approved by the FDA for this purpose. These medications are approved for the management of type 2 diabetes, where they work by improving the body's sensitivity to insulin.

Some PCOS patients who fail to ovulate in response to either clomiphene or metformin alone may respond when the two medications are used in combination. In a large study sponsored by the National Institute of Child Health and Development (NICHD), metformin alone was less successful in helping couples conceive than clomiphene alone or metformin plus clomiphene. Gastrointestinal side effects of metformin are common and include nausea, vomiting and diarrhea. Since metformin therapy is associated with liver dysfunction, and rarely, a severe condition called lactic acidosis, liver and kidney function tests should be performed periodically. Other diabetic drugs that improve insulin sensitivity, such as rosiglitazone and pioglitazone, also have been used for this purpose. For more information, please see the ASRM Fact Sheet titled *Insulin Sensitizing Agents and PCOS*.

Gonadotropins

Gonadotropins are fertility medications that contain FSH or LH alone or in combination. In contrast to clomiphene, which is given by mouth, gonadotropins are given by injections. A related medication is hCG, which is structurally similar to LH and mimics the natural LH surge. There are a variety of commercially available gonadotropin preparations, and others are in various stages of research and development. Because of rapid changes in the international marketplace, the medications named in the sections below may not represent all of the formulations available in the United States and worldwide. Gonadotropins often are prescribed for anovulatory women who have tried clomiphene without success. They are also used to help women whose pituitary glands do not produce adequate amounts of FSH and LH. Additionally, gonadotropins are used to induce development of multiple follicles for fertility treatments, such as superovulation-IUI and IVF.

Most physicians begin gonadotropin treatment on day two or three of the menstrual cycle. For non-IVF cycles, the usual starting dose is 75 to 150 units injected daily. Injections usually are administered over a period of seven to 12 days, but may be extended if the ovaries are slow to respond. The follicle size is monitored with ultrasound, and the blood estrogen level may be measured frequently throughout treatment. If estradiol levels and follicular monitoring indicates that the ovaries are not responding to gonadotropins, the dose may be increased. The goal is to achieve one or more mature follicles and an appropriate estrogen level, so that ovulation can be triggered by an hCG injection. If too many follicles develop, or if the estrogen level is too high, the physician may decide to withhold the hCG injection rather than risk the higher likelihood of *ovarian hyperstimulation syndrome (OHSS)* or a high-order multiple pregnancy.

Human Chorionic Gonadotropin (hCG)

Produced in pregnant women by the placenta and extracted from the urine, hCG is similar in chemical structure and function to LH. As such, in a manner similar to the natural LH surge, an injection of hCG can cause the dominant follicle to release its egg. The physician may use ultrasound and blood estrogen levels to determine the day on which to administer hCG. *Ovulation* will usually occur about 36 hours after hCG is administered. Human chorionic gonadotropin is routinely used to trigger ovulation when gonadotropins are used to induce ovulation. Human chorionic gonadotropin may also be used to trigger ovulation when clomiphene is used to induce ovulation, particularly when a mid-cycle LH surge cannot be reliably detected. A pregnancy test (which measures hCG in the urine or blood) may be falsely positive if performed less than 10 days after hCG is administered.

Side effects of gonadotropins

There are potential risks and complications associated with the use of gonadotropins. Side effects should be discussed prior to taking these medications. Despite intensive monitoring, up to 30% of gonadotropin-stimulated pregnancies are multiple. Of the multiple pregnancies, about two-thirds are twins and one-third are triplets or more. Premature delivery is a known risk for multiple pregnancies. The greater the number of fetuses in the uterus, the greater the risk of premature delivery. Premature delivery can subject the newborn to complications such as severe respiratory distress, intracranial hemorrhage, infection, cerebral palsy, and

death. Some patients pregnant with triplets or more choose to undergo a procedure known as *multifetal pregnancy reduction* in an effort to decrease these risks.

In addition to problems associated with high order multiple gestation, another serious side effect of gonadotropin therapy is ovarian hyperstimulation syndrome (OHSS), in which the ovaries become swollen and painful. In severe cases, fluid accumulates in the abdominal cavity and chest. In about 2% of gonadotropin cycles, hyperstimulation may be severe enough to require hospitalization. Careful monitoring of ovulation induction cycles with the use of ultrasound and/or measurement of serum estradiol levels, in conjunction with adjustment of gonadotropin dosage, will enable the physician to identify risk factors and prevent most cases of severe OHSS. When serum estradiol levels are rapidly rising and/or too high, or an excessive number of ovarian follicles develop, one method of best prevention is to withhold further gonadotropin stimulation and delay hCG administration until estradiol levels plateau or decline. Alternately, hCG can be withheld so that ovulation fails to occur, thereby lessening the severity of OHSS.

Other potential side effects of gonadotropin treatment include breast tenderness, swelling or rash at the injection site, abdominal bloating, mood swings, and slight twinges of abdominal pain. Some women experience mood swings during gonadotropin therapy, although usually less severe than those that occur with clomiphene. It is difficult to separate the emotional changes due to the dramatic hormone shifts during gonadotropin therapy from the stress associated with this treatment. Regardless of the cause, a change in mood can be expected during gonadotropin therapy.

Bromocriptine and Cabergoline

Some women ovulate irregularly because their pituitary glands secrete too much *prolactin*. Increased blood levels of prolactin inhibit the release of FSH and LH, and therefore stop ovulation. The prolactin level is elevated in some women because the prolactin producing cells in the pituitary are hyperactive or form an *adenoma*. High prolactin levels *(hyperprolactinemia)* also can result from the use of certain drugs such as tranquilizers, hallucinogens, painkillers, alcohol, and, in rare cases, oral contraceptives. Disease of the kidney or thyroid may also raise prolactin levels.

Hyperprolactinemia often is treated with bromocriptine (brand name: Parlodel) or cabergoline (brand name: Dostinex) which act by reducing the amount of prolactin released by the pituitary gland. Blood prolactin levels return to normal in 90% of patients who take these medications. Bromocriptine is taken orally each day until the prolactin level is normal. It can also be administered vaginally. Cabergoline is taken as one to two tablets twice each week. Of the women treated, approximately 85% will ovulate and can become pregnant if no other causes of infertility are present. Bromocriptine and cabergoline treatments are usually discontinued during pregnancy. Women who fail to ovulate even after their prolactin levels are normal may be given clomiphene or gonadotropins along with bromocriptine and cabergoline. Possible side effects of bromocriptine and cabergoline include nasal congestion, fatigue, drowsiness, headaches, nausea, vomiting, fainting, dizziness and decreased blood pressure. For most patients, adjusting the dosage can eliminate these side effects. Some physicians start their patients on a very low dose and increase it gradually in an effort to prevent side effects. The risk of multiple pregnancies is not increased as a result of bromocriptine or cabergoline therapy.

Gonadotropin-releasing Hormone (GnRH)

Gonadatropin-releasing hormone is released from the hypothalamus in small amounts about once every 90 minutes. The pulsatile release of GnRH from the hypothalamus into the blood stream stimulates the pituitary gland to secrete LH and FSH. If GnRH is not being released properly, it can be given in a pulsatile manner by a special drug delivery system that includes a belt holding a lightweight pump. The pump delivers a small volume of fluid every 60 to 90 minutes through a needle placed beneath the skin (usually in the abdomen) or into a blood vessel. The risk and complications of GnRH, such as multiple births and ovarian hyperstimulation syndrome, are quite small.

GnRH Analogs (Agonists and Antagonists)

GnRH analogs are synthetic hormones similar to natural GnRH, but which are chemically modified. Leuprolide acetate, nafarelin acetate, and goserelin acetate are *GnRH agonists*. The normal pulsatile rhythmic release of GnRH from the hypothalamus stimulates the pituitary gland to secrete LH and FSH. At present, GnRH is not available for this use in the United States. However, when a woman takes a GnRH agonist, her pituitary gland is exposed to a constant, rather than a pulsatile, pattern of synthetic GnRH.

After an initial acceleration in LH and FSH production, the production of FSH and LH by the pituitary gland declines and spontaneous ovulation is usually prevented.

Ganirelix and cetrorelix acetate are *GnRH antagonists*, which suppress the production of FSH and LH without the initial stimulation. Both agonists and antagonists are ineffective when taken orally. GnRH analogs often are used to prevent spontaneous ovulation when gonadotropins are given to women undergoing IVF. Both the GnRH agonist and antagonist can prevent the undesired secretion of LH, which can cause the follicles to release their eggs before they are harvested. Many infertility specialists believe that the addition of GnRH analogs during ovarian stimulation for IVF yields more mature eggs for fertilization and, therefore, more embryos for transfer. The patient taking a GnRH antagonist or agonist long term often has temporary symptoms of menopause, including hot flashes, mood swings, and vaginal dryness. In addition, headaches, insomnia, decreased breast size, pain during intercourse, and bone loss may occur. These side effects are temporary, and the effect on the pituitary is reversible after GnRH agonists and GnRH antagonists are discontinued. In the course of ovulation induction, these side effects are rare.

LONG-TERM RISKS OF OVULATION DRUGS

After years of clinical use, physicians can advise patients confidently that clomiphene citrate and gonadotropins are not associated with an increased risk of birth defects. It has been suggested that women taking ovulation-inducing drugs such as clomiphene and gonadotropins may be at increased risk for ovarian cancer. Recent studies and re-analysis of earlier studies do not support this connection.

CONCLUSION

Lack of ovulation is very treatable. As a result of treatment, many infertile couples of achieving their goal of having a child.

GLOSSARY

Adenoma. A type of benign (non-cancerous) pituitary tumor that may secrete excess amounts of prolactin or other hormones.

Amenorrhea. Absence of menstrual periods.

Anovulation. A condition in which a woman rarely or never ovulates.

Biopsy. A tissue sample taken for microscopic examination.

Bromocriptine. A drug used to suppress the pituitary gland's production of prolactin. Parlodel® is a brand name.

Cabergoline. A drug used to suppress the pituitary gland's production of prolactin.

Cervix. The narrow, lower end of the uterus where it opens into the vagina.

Clomiphene citrate. An antiestrogen drug used to induce ovulation.

Controlled ovarian stimulation (COS). Administration of fertility medications in order to achieve the development of two or more mature follicles. Also called superovulation.

Corpus luteum. A mature follicle that has collapsed after releasing its egg at ovulation. The corpus luteum secretes progesterone and estrogen during the second half of a normal menstrual cycle. The secreted progesterone prepares the lining of the uterus (endometrium) to support a pregnancy.

Embryo. The earliest stage of human development after a sperm fertilizes an egg.

Endometrium. Uterine lining that sheds monthly to produce a menstrual period.

Estradiol. The main estrogen (hormone) produced by the follicular cells of the ovary.

Estrogen. The female sex hormone produced by the ovaries that is responsible for the development of female sex characteristics. Estrogen is largely responsible for stimulating the uterine lining to thicken during the first half of the menstrual cycle in preparation for ovulation and possible pregnancy. It is also important for healthy bones and overall health. A small amount of this hormone is also made in the male testes.

Fallopian tubes. A pair of hollow tubes attached one on each side of the uterus. The egg travels from the ovary to the uterus through narrow passageways in the middle of these tubes.

Fimbriae. The finger-like projections of the fallopian tubes that sweep over the ovary and move the egg into the tube.

Follicle. A fluid-filled cyst located just beneath the surface of the ovary, containing an egg (oocyte) and cells that produce hormones. The sac increases in size and volume during the first half of the menstrual cycle, and 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 estrogen. In the male, FSH is the pituitary hormone which travels through the bloodstream to the testes and helps stimulate them to manufacture sperm. FSH can also be given as a medication.
Follicular phase. The first half of the menstrual cycle (beginning on day one of bleeding) during which the dominant follicle secretes large amounts of estrogen.
Gonadotropin-releasing Hormone (GnRH). The natural hormone secreted by the hypothalamus that prompts the pituitary gland to release FSH and LH into the bloodstream. This in turn stimulates the ovaries to produce estrogen, progesterone, and to ovulate.
GnRH Agonists. Synthetic hormones similar to the naturally occurring gonadotropin-releasing hormone (GnRH) that initially stimulate and then subsequently decrease FSH and LH secretion from the pituitary gland.
GnRH Antagonists. Synthetic hormones that directly decrease FSH and LH secretion from the pituitary gland.
Human chorionic gonadotropin (hCG). A hormone produced by the placenta during pregnancy that mimics the LH surge. It is often used with clomiphene or hMG to cause ovulation.
Human menopausal gonadotropin (hMG). An ovulation drug containing a mixture of follicle stimulating hormone and luteinizing hormone derived from the urine of postmenopausal women.
Hyperprolactinemia. High levels of prolactin in the bloodstream.
Hypothalamus. A thumb-sized area in the brain that controls many functions of the body, regulates the pituitary gland, and releases GnRH.
Hysterosalpingogram. An X-ray performed after dye is injected into the uterus and fallopian tube to determine if both fallopian tubes are open and if the shape of the uterine cavity is normal.
In vitro fertilization (IVF). A method of assisted reproduction that involves surgically removing an egg from the woman's ovary and combining it with sperm in a laboratory dish. If the egg is fertilized, resulting in an embryo, the embryo is transferred to the woman's uterus.

Insemination. The deposit of semen through a syringe within the uterine cavity or cervix to facilitate fertilization of the egg.
Laparoscopy. A surgery performedin which a thin camera is inserted into the abdomen through a small incision to inspect the condition of the pelvic organs.
LH surge. The secretion, or surge, of large amounts of luteinizing hormone (LH) by the pituitary gland. This surge is the stimulus for ovulation to occur.
Luteal phase. The second half of the menstrual cycle after ovulation when the corpus luteum secretes large amounts of progesterone.
Luteal phase defect. A shorter than normal luteal phase or one with lesser progesterone secretion despite a normal duration.
Luteinizing hormone (LH). The hormone that triggers ovulation and stimulates the corpus luteum to secrete progesterone.
Multifetal pregnancy reduction. Also known as selective reduction. A procedure to reduce the number of fetuses in the uterus. This procedure may be considered for women who are pregnant with multiple fetuses. As the risk of extreme premature delivery, miscarriage (spontaneous abortion), and other problems increases with the number of fetuses present, this procedure may be performed in an attempt to prevent the entire pregnancy from aborting.
Oligo-ovulatory. A term describing a woman who ovulates infrequently.
Ovarian hyperstimulation syndrome (OHSS). A possible side-effect of treatment with human menopausal gonadotropin in which the ovaries become painful and swollen, and fluid may accumulate in the abdomen and chest.
Ovarian reserve. A woman's fertility potential in the absence of specific pathophysiologic changes in her reproductive system. Diminished ovarian reserve is associated with depletion in the number of eggs and worsening of oocyte quality.
Ovulation. The expulsion of a mature egg from its follicle in the outer layer of the ovary. It usually occurs on approximately day 14 of a 28-day cycle.
Pituitary gland. A small gland just beneath the hypothalamus that secretes follicle stimulating hormone and luteinizing hormone, which stimulate egg maturation and hormone production by the ovary.
Polycystic ovary syndrome (PCOS). A condition characterized by chronic anovulation, excessive ovarian production of testosterone and/or ovaries with many small cystic follicles. Symptoms may include

irregular or absent menstrual periods, obesity, infertility, excessive hair growth, and/or acne.

Progesterone. A female hormone 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 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.

Progestin. A synthetic hormone that acts similar to progesterone.

Prolactin. A pituitary hormone that stimulates milk production and inhibits ovulation by inhibiting FSH and LH release.

Superovulation. Administration of fertility medications in order to achieve the development of two or more mature follicles. Also called controlled ovarian stimulation.

Ultrasound. High frequency sound waves that produce an image of internal organs on a monitor screen.

Uterus (womb). The muscular 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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AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE
1209 MONTGOMERY HIGHWAY
BIRMINGHAM, ALABAMA 35216-2809
(205) 978-5000 • ASRM@ASRM.ORG • WWW.ASRM.ORG