zyme that is largely responsible for producing estrogen in body tissues outside of the ovaries. These drugs include anastrozole (Arimidex) and letrozole (Femara). These drugs are used for treating breast cancer and are being investigated for stimulating ovulation in infertile women. Although letrozole is not approved for treatment of infertility, it has become widely used for this purpose in recent years.

Progesterone. Progesterone is a hormone that is produced by the body during the menstrual cycle. Progesterone drugs are sometimes given to women who have experienced frequent miscarriages (a possible sign of progesterone deficiency). A progesterone drug may also be given after egg retrieval during an in vitro fertilization (IVF) cycle to help thicken the uterine lining (endometrium) so it can better hold the egg following implantation.

Tamoxifen. Tamoxifen (Nolvadex) is a drug known as a selective estrogen-receptor modulator

(SERM). It is used to treat or prevent breast cancer in certain women. It is also being studied in fertility treatments to induce ovulation. Tamoxifen works in a similar to clomiphene but may pose more health hazards, including a risk for blood clots and uterine cancer.

Information contained in this booklet is meant for informational purposes only and should not substitute the visit to your doctor nor his/her advice for your health care.

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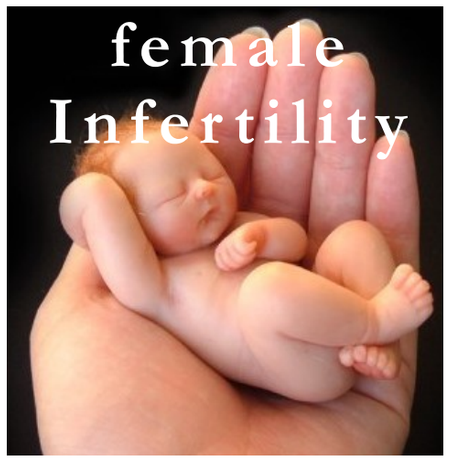
MANSOOR MEDICAL

Causes of female Infertility



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Treatment for infertility should first address any underlying medical condition that may be contributing to fertility problems. Drugs, surgery, or both may be used to treat these conditions. Surgery may also be used to repair blockage in fallopian tubes.

Fertility Treatment Approaches

Several approaches are used to treat infertility:

- Lifestyle measures (healthy lifestyle, planning sexual activity with ovulation cycle, managing stress and emotions)
- Drugs to induce ovulation, such as clomiphene and gonadotrophins
- Assisted reproductive technologies (ART) such as in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI)

This brochure will address the first two approaches.

Special Considerations for Patients with Cancer

Women who are undergoing cancer treatments and who want to become pregnant should see a reproductive specialist to discuss their options. According to the American Society of Clinical Oncology's guidelines, the fertility preservation method with the best chance of success is embryo cryopreservation. This procedure involves harvesting a woman's eggs (oocytes), followed by in vitro fertilization and freezing of embryos for later use. Other treatments under investigation include egg preservation, collecting and freezing unfertilized eggs, removing and freezing a part of the ovary for later reimplantation, and using hormone therapy to protect the ovaries during chemotherapy. Women may be able to access these investigational approaches through enrolling in clinical trials.

Medications

Fertility drugs are often used alone as initial treatment to induce ovulation. If they fail as sole therapy, they may be used with assisted reproductive procedures, such as in vitro infertilization, to produce multiple eggs, a process called *superovulation*.

According to the American Society for Reproductive Medicine, fertility drugs can be divided into three main categories:

- *Medications for Ovarian Stimulation*. Clomiphene (Clomid, Serophene); letrozole (Femara), follicle stimulating hormone (FSH) [Follistim, Gonal-F, Bravelle]; human menopausal gonadotrophin (hMG) [Humegon, Repronex, Menopur]; luteneizing hormone (LH) [Luveris]
- *Medications for Oocyte Maturation*. Human chorionic gonadotropin (hCG) [Profasi, APL, Pregnyl, Novarel, Ovidrel]
- *Medications to Prevent Premature Ovulation*. GnRh agonists (Lupron and Synarel); Gn RH antagonists (Antagon, Cetrotide).

Clomiphene

Clomiphene citrate (Clomid, Serophene) is usually the first fertility prescribed for women with infrequent periods and long menstrual cycles. Unlike more potent drugs used in superovulation, clomiphene is gentler and works by blocking estrogen, which tricks the pituitary into producing follicle-stimulating hormone (FSH) and luteinizing hormone (LH). This boosts follicle growth and the release of the egg. Clomiphene can be taken orally, is relatively inexpensive, and the risk for multiple births (about 5%, mostly twins) is lower than with other drugs.

Women with the best chances for success with this drug are those who have the following conditions:

- Polycystic ovarian syndrome (PCOS)

Infertility …. Treatment Options

- Ability to menstruate but irregular menstrual cycle

Women with poorer chances of success with this drug have the following conditions:

- Infertility but with normal ovulation
- Low estrogen levels
- Premature ovarian failure (early menopause)

One or two tablets are taken each day for 5 days, usually starting 2 - 5 days after the period starts. If successful, ovulation occurs about a week after the last pill has been taken. If ovulation does not occur, then a higher dose may be given for the next cycle. If this regimen is not successful, treatment may be prolonged or additional drugs may be added. Doctors usually do not recommend more than 6 cycles.

Clomiphene often reduces the amount and quality of cervical mucus and may cause thinning of the uterine lining. In such cases, other hormonal drugs may be given to restore thickness. Other side effects of clomiphene include ovarian cysts, hot flashes, nausea, headaches, weight gain, and fatigue. There is a 5% chance of having twins with this drug, and a slightly increased risk for miscarriage.

Gonadotropins

If clomiphene does not work or is not an appropriate choice, gonadotropin drugs are a second option. Gonadotropins include several different types of drugs that contain either a combination of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), or only FSH. Whereas clomiphene works indirectly by stimulating the pituitary gland to secrete FSH, (which prompts follicle production), gonadtropin hormones directly stimulate the ovaries to produce multiple follicles.

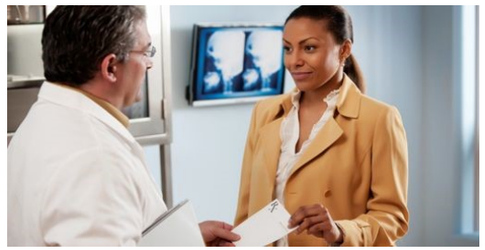
Gonadotropins are given by injection. (Your doctor may show you how to self-administer the injection.) Gonadotropins include:

- Human Menopausal Gonadtropins (hMG), also called menotropins
- Human Chorionic Gonadotropins (hCG)
- Follicle Stimulating Hormone (FSH)
- Gonadotropin-releasing hormone (GnRH) analogs, which include GnRH agonists and GnRH antagonists

Gonadotropin drugs are either natural compounds extracted from urine or synthetic compounds that are genetically engineered in a laboratory using recombinant DNA.

Human Menopausal Gonadotropin (hMG). HMG drugs, also called menotropins, contain a mixture of both FSH and LH. These drugs (Menopur, Repronex, Humegon) are all derived from the urine of postmenopausal women. HMG is administered as a series of injections 2 - 3 days after the period starts. Injections are usually given for 7 - 12 days, but the time may be extended if ovulation does not occur. In such cases, a shot of human chorionic gonadotropin (hCG) may trigger ovulation.

Human Chorionic Gonadotropin (hCG). Human chorionic gonadotropin (hCG) is similar to LH. It mimics the LH surge, which stimulates the follicle to release the egg. Natural hCG drugs, derived from the urine of pregnant women, include Pregnyl, Profasi, Novarel, and APL. Ovidrel is the only available genetically modified hCG drug. Ovidrel has fewer side effects at the injection site, and its quality can be better controlled than the natural drugs. It is generally used after hMG or FSH to stimulate the final maturation stages of the follicles. Ovulation, if it occurs, does so about 36 - 72 hours after administration.



Follicle Stimulating Hormone (FSH). Urofollitropin (Bravelle, Fertinex) is a purified form of FSH, derived from the urine of postmenopausal women. Follitropin drugs (Gonal-F, Follistim) are synthetic versions of FSH. These FSH drugs are sometimes given in combination with an hCG drug.

GnRH Analogs (Agonists or Antagonists). Gonadotropin-releasing hormone (GnRH) is a hormone produced in the hypothalamus part of the brain. GnRH stimulates the pituitary gland to produce LH and FSH. GnRH analogs are synthetic drugs that are classified as either agonists or antagonists. They are similar to natural GnRH but have very different actions. While natural GnRH stimulates LH and FSH, these drugs actually prevent the LH and FSH surge that occurs right before ovulation. This action helps prevent the premature release of the eggs before they can be harvested for assisted reproductive technologies.

- GnRH agonists include leuprolide (Lupron), nafarelin (Synarel), and goserelin (Zoladex).
- GnRH antagonists include ganarelix (Antagon) and cetrorelix (Cetrotide). GnRH antagonists suppress FSH and LH more than GnRH agonists, and they may require fewer injections.

Complications of Superovulation

Multiple Births. Overproduction of follicles can lead to ovarian enlargement. This event increases the risk for multiple births. There is a 25% chance of multiple births (about 17% for twins and 8% for triplets and or more).

Ovarian Hyperstimulation Syndrome. The most serious complication with superovulation is ovarian hyperstimulation syndrome (OHS), which is associated with the enlarged ovary (although the precise cause is unknown). This can result in dangerous fluid and electrolyte imbalances and endanger the liver and kidney. OHS is also associated with a higher risk for blood clots. In rare cases, it can be fatal. Symptoms include abdominal bloating, nausea, vomiting, and shortness of breath.

Bleeding and Rupture of Ovarian Cysts. Overproduction of follicles, if unchecked, may result in bleeding and rupture of ovarian cysts.

Cancer Concerns. There has been concern that clomiphene and gonadotropins may increase the risks for ovarian and breast cancer. Most evidence to date does not indicate that ovulation-stimulating drugs increase the risks for these types of cancers. Some studies suggest that clomiphene, which is chemically related to the breast cancer drug tamoxifen, may actually decrease the risk for breast cancer.

Other Drugs Used or Under Investigation

Letrozole and Aromatase Inhibitors. Aromatase inhibitors block aromatase, an en-