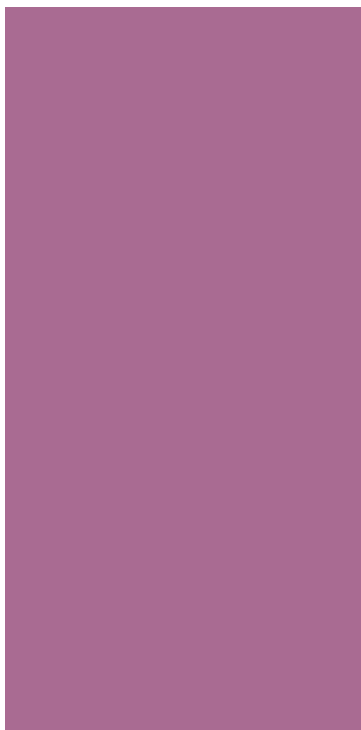
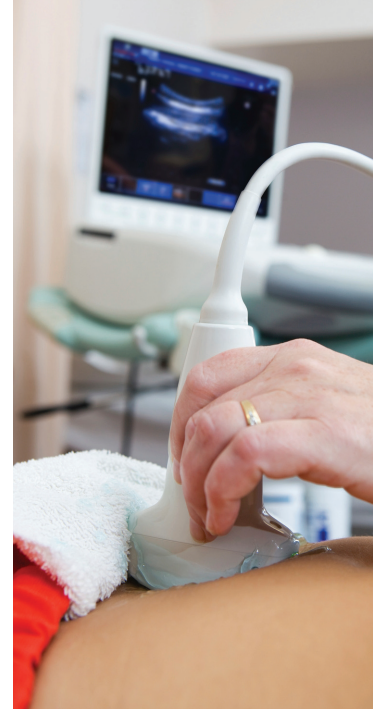


The Reproductive Science Institute
of Suburban Philadelphia, P.C., Explains...

Assisted Reproductive Techniques



Reproductive Science Institute
of Suburban Philadelphia, P.C.

Dear Patient:

If you're like most individuals, you're unfamiliar with treatment cycles associated with assisted reproductive techniques (referred to as "ART" by the medical community.) That's why we at the Reproductive Science Institute have created this short booklet.

Throughout the following pages, you'll learn more about:

- Assisted Reproductive Techniques (ART)
- Intrauterine Insemination (IUI)
- In Vitro Fertilization (IVF)
- An ART Stimulated Cycle
- Side Effects and Personal Considerations

All information should be considered an overview. As such, it is intended to be supplemented with discussions with your physician, a critical component in providing you with a clear and realistic picture of your own medical situation.

To find out more about ART, please visit our website at www.RSIinfertility.com.

Thank you for choosing the Reproductive Science Institute.

ART: WHAT YOU NEED TO KNOW

The overarching aim of assisted reproductive technology (ART) is to help achieve a pregnancy.

By definition, ART is any procedure that is utilized to increase monthly pregnancy rates. ART may be limited to intrauterine insemination (IUI) or ART may involve more complex procedures such as in vitro fertilization (IVF). In general, ART is considered a viable medical option when there are both correctable and non-correctable or unknown medical problems that make it unlikely or impossible to achieve a pregnancy through natural intercourse.

Since the introduction of IVF in the late 1970s, there has been an ongoing increase in the number of related procedures that are available to couples. Following an extensive individual evaluation, the best course of ART will be recommended by your physician.

There are a number of variations of assisted reproduction, but all involve working with oocytes (eggs), sperm, and/or embryos in the fresh or frozen condition outside of the body.

Donor sperm is widely used at the Reproductive Science Institute. Patients may purchase and order donor sperm on their own, or select samples from several cryobanks that provide donor profiles to RSI.

INTRAUTERINE INSEMINATION (IUI)

Intrauterine insemination (IUI) (sometimes used interchangeably with the term “artificial insemination”) refers to a procedure where washed or prepared sperm is introduced through a sterile plastic catheter into the uterus through the cervix around the time of ovulation.

If no fertility drugs are used and a patient has normal cycles, ovulation can be predicted by monitoring urinary LH (Luteinizing Hormone). Monitoring of urinary LH can be accomplished through the use of a urine LH kit. Such kits are available over-the-counter at pharmacies. The IUI is typically performed 1-2 days after the LH surge.

If fertility drugs are used, monitoring of the ovarian stimulation levels will begin with the onset of the cycle. The monitoring will continue until the end of the cycle, similar to an IVF cycle, which includes blood tests and ultrasound examination.

Potential Side Effects of IUI:

- Pelvic infection
- Uterine cramping
- Bleeding
- Mild discomfort
- Perforation of the uterus (rare)
- Multiple gestations may also occur as a result of IUI following induction of ovulation
- Other side effects

IN VITRO FERTILIZATION (IVF)

In vitro fertilization (IVF) is fertilization of an egg outside the body. An ART procedure, IVF is recommended based on a patient’s medical history or repeated unsuccessful attempts of other treatment options.

Originally designed to bypass diseased fallopian tubes, the utilization of IVF has expanded as a fertility treatment for male factor infertility, endometriosis, unexplained infertility and the desire to be aggressive with patients of advanced reproductive age.

Variations of IVF are the basis for many of the related ART procedures, such as donor egg, donor embryo, gestational surrogacy and pre-implantation genetic testing.

Potential Side Effects of IVF:

- Menopausal symptoms (e.g., hot flashes, headaches, mood swings)
- Cramping
- Stomach swelling/pain
- Nausea/Vomiting
- Rapid weight gain
- Shortness of breath

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- Ectopic pregnancy
- Other side effects

STIMULATED CYCLE: OOCYTE (EGG) DEVELOPMENT AND MONITORING FOR IUI OR IVF

A woman's body can normally produce only one egg that is released from an ovary for fertilization each month. To increase the chances for successful pregnancy through ART, women are given certain medications to control their normal menstrual cycles and help their bodies produce more than one egg during any given cycle.

During a normal menstrual cycle, a woman's body produces estrogen and progesterone (steroid hormones), as well as follicle stimulating hormone (FSH) and luteinizing hormone (LH).

FSH is the primary hormone involved in recruiting egg production. The body's own estrogen production is a consequence of this activity.

LH is involved in the oocyte's response to FSH.

In a stimulated ART cycle, hormones are given exogenously at slightly higher than natural levels to stimulate egg production. Most of the injectable medications that patients use are forms of FSH, but may be a mixture of FSH and LH.

FSH and LH Medications and Their Common Side Effects

A highly purified form of FSH that we at the Reproductive Science Institute use extensively is referred to as recombinant FSH. This form of FSH (Gonal-F, Follistim) has been artificially manufactured and is approved by the Food and Drug Administration for use in IVF protocols.

Some FSH products (Repronex, Menopur, Humegon) may also contain traces of LH. These products, along with hCG (Profasi, Pregnyl, Ovidrel) and clomiphene citrate are approved for ovulation induction in women who do not ovulate and their usage for ART is a natural extension of this approval.

Most of the side effects of the aforementioned drugs are minor and temporary, involving discomfort, but not usually requiring continuing or unusual medical intervention. They may include:

- Nausea
- Headache
- Mood swings
- Abdominal bloating
- Abdominal discomfort

Serious complications of these medications, with the exception of multiple births, are rare. The manufacturers of these prescription drugs advise that serious pulmonary conditions and thromboembolic (blood clot) events have been reported in conjunction with the use of ovarian stimulation medication. Additionally, some patients might have a hypersensitivity to such drugs.

The medications used for IVF or injectable IUI cycles to recruit the production of numerous eggs within ovarian follicles are proteins that are naturally found in the body.

Symptoms of generalized rash or redness, swelling or pain in your legs, or difficulty breathing should be reported to your doctor immediately.

Lupron and Synarel are medications that are used to suppress natural hormone levels prior to initiation of an ART/IVF cycle and administration of controlled dosages of medications. This process of suppression is called down-regulation, or pituitary down-regulation.

Lupron and Synarel are approved for pituitary down-regulation, but not specifically for ART. Their temporary side effects may include

- Headache
- Hot flashes
- Mood swings
- Loss of libido
- Insomnia

Ganirelix is another medication sometimes used during an IVF or IUI cycle to prevent the premature release of an egg (ovulation).

It is also sometimes difficult to rule out the possibility of a pregnancy even when it seems that normal menstruation has occurred. For this reason, women may be asked to have a pregnancy test prior to commencing a cycle. Additionally, couples may be asked to refrain from intercourse, or use barrier protection at certain times of the woman's cycle.

After a Stimulated Cycle Begins

Once a patient begins a stimulated cycle and administer the FSH medication, she will begin a regular monitoring process whereby every few days she will be required to come into the office for blood work and ultrasound of her ovaries.

This is how the Reproductive Science Institute's specialists measure the response of a woman's body to the medications and also the production of follicles which contain eggs.

Note: A woman's initial dosage of medication may be changed or supplemented during this monitoring period that lasts for 9-11 days (in most cases.)

When the woman's blood hormone levels and ultrasound findings indicate adequate follicles, ovulation will be triggered. Subsequently, she will undergo an IUI or IVF egg retrieval depending on the ART procedure she has initiated.

Administration of Intramuscular and Subcutaneous Injections and Their Side Effects

RSI teaches patients and their partners (or another person) how to administer intramuscular (in the muscle (IM)) and subcutaneous (beneath the skin) injections. Because the medications are given by injection, bruising, pain or swelling at the injection site is fairly common. Allergy to the medications resulting in a rash or hives occurs occasionally.

It is important for patients to carefully follow medication instructions, such as taking the prescribed dosage at the prescribed time. Numerous eggs within ovarian follicles are proteins that are naturally found in the body.

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The injectable drugs may occasionally cause the development of ovarian cysts (non-cancerous, fluid-filled structures in the ovaries); in rare instances these may need to be drained or removed surgically, in which case hospitalization may be required. Though the removal of an ovarian cyst can result in the loss of an ovary, though such a loss is rare.

It is also possible for an ovarian cyst to rupture, causing a brief episode of pain.

Under rare circumstances, the rupture of an ovarian cyst may be associated with sudden bleeding and require surgery and/or blood transfusion(s). Such acute bleeding is very unusual.

Multiple Pregnancies and Preterm Labor

Another potential complication of the ART stimulated cycle is multiple pregnancy (twins and higher). A multiple pregnancy is more complicated and may require prolonged bedrest.

There are alternatives to limit or reduce the risk of multiple pregnancies, including cycle cancellation, not administering hCG, conversion to IVF and limiting the number of embryos replaced. Another alternative is fetal reduction.

Preterm labor is also more likely and depending on the timing of the delivery, there may be serious complications for the baby involving lungs, brain, vision, growth, and development.

Cancellation of the ART Cycle

Problems do occur which prevent the completion of an ART cycle.

A physician may stop treatment prior to the retrieval of eggs for numerous medical reasons. The most likely reasons for such a cancellation is a patient's low response (few follicles, low estrogen levels) to the ovulation induction drugs. Such cancellations occur more frequently in women over age 40. In some cases, the patient may then proceed to have an IUI that cycle.

Ovarian Cancer

In November of 1992, a published study addressed a potential risk of ovarian cancer associated with the use of certain medications for ovarian stimulation.

Since that time, the consensus of medical opinion on the issue, as voiced by the Society of Assisted Reproductive Technology (SART) and the American Society for Reproductive Medicine (formerly the American Fertility Society), is that there is no conclusive evidence of risk. As part of patient counseling, all patients are advised to discuss this issue with their physicians.

Ultrasound examinations are used to visualize the ovaries and the uterus and to help predict the timing of ovulation. Occasionally there may be some discomfort; however, generally ultrasounds are considered harmless and painless. There is no known risk associated with ultrasound.

OVARIAN HYPERSTIMULATION SYNDROME (OHSS)

The process of in vitro fertilization (IVF) involves the intentional controlled overstimulation of the ovaries in order to obtain an optimal number of mature eggs. It is possible that this may result in a dramatic increase in the size of the ovaries and leakage of fluid into the pelvis/abdomen, causing a number of symptoms referred to as OHSS.

Symptoms, if they occur, are related to the significant enlargement of the ovaries and usually follow 5 to 7 days after ovulation (or IVF retrieval), but may also occur after transfer or with pregnancy.

OHSS is usually managed by bed rest and hydration at home. In some instances, hospitalization may be necessary with intravenous fluid replacement and drainage of abdominal fluid collections.

As a result, when a patient exhibits signs and symptoms which suggest that there is the probability of severe hyperstimulation, a cycle may be canceled. In most cases of cancellation, it is possible to attempt another cycle with adjusted levels of medication.

OHSS is also possible in an IUI cycle, but much less common.

Warning signs of OHSS include:

- Nausea and vomiting
- Weight gain of 2 or more pounds/day for 2 days or more
- Pelvic pain
- Difficulty breathing
- Severe abdominal bloating
- Decreased urination despite usual fluid intake

It is considered an **emergency** if a patient experiences any one or a combination of these symptoms.