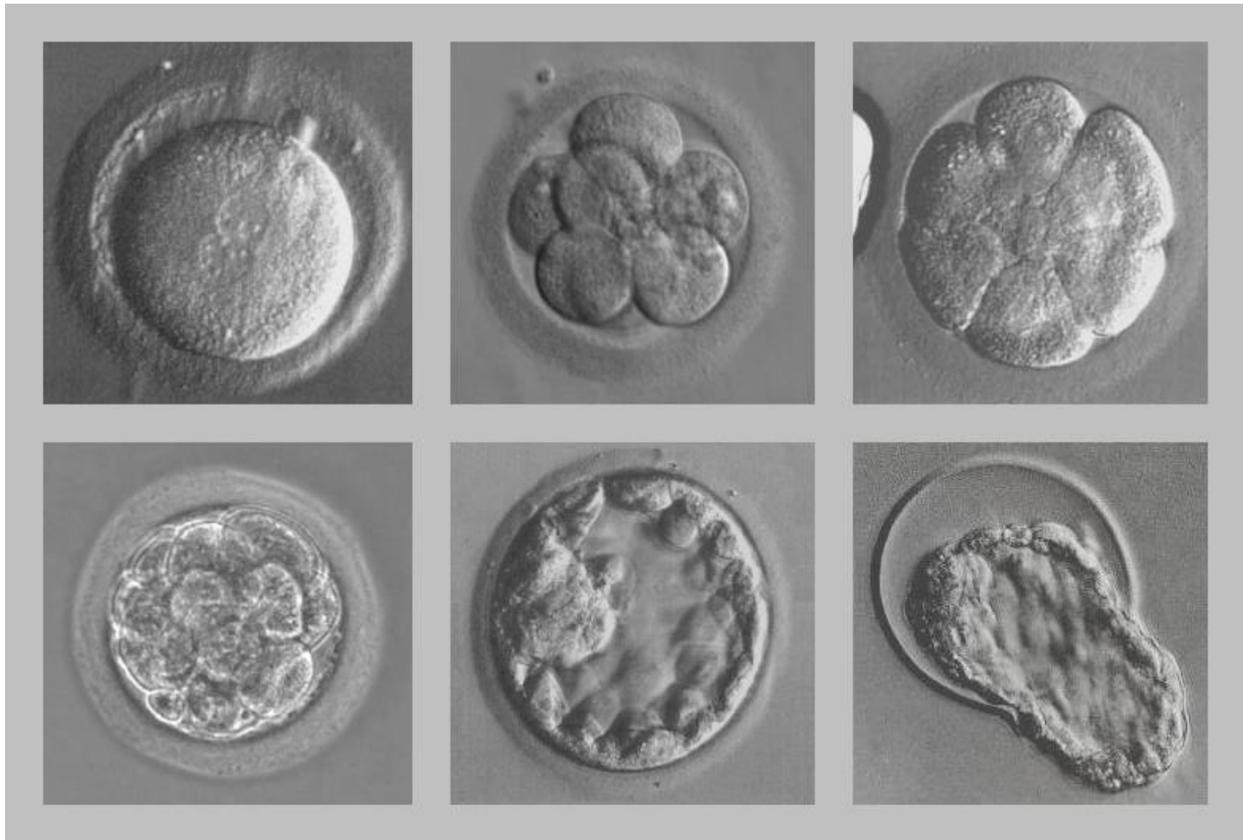




Center for Reproductive Medicine



**Patient Guide to
Assisted Reproductive Technologies**

(336) 716-6476

www.wakehealth.edu/ivf

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Advanced Reproductive Technologies (ART)

Advanced Reproductive Technologies (ART) is a term used to describe a number of various technologies that have been developed to assist patients in becoming pregnant. These technologies include in vitro fertilization-embryo transfer (IVF-ET), frozen embryo transfer (FET), and micromanipulation. Micromanipulation refers to special techniques used by the ART laboratory to manipulate sperm, eggs, and/or embryos. These techniques include; intracytoplasmic sperm injection (ICSI), assisted hatching (AH), and preimplantation genetic diagnosis (PGD).

This booklet is divided into two sections. The first section is a general review of the different ART technologies employed here at the Wake Forest University Center for Reproductive Medicine. Section II, contains specific instructions related to the IVF cycle, as well as a glossary. It is important that you read this booklet in its entirety and ask questions regarding any of the information presented.

ART/IVF CANDIDATES

Most patients who undergo ART have tried other less complex methods for treating their infertility. Although ART was originally developed to treat infertility caused by tubal disease or blockage; today it is an effective treatment for almost every cause of infertility. ART may be used as first-line therapy for patients with severe tubal disease, severe endometriosis, advanced age, or in couples with severe male factor infertility. It can also be used for patients who may be carriers for genetic disorders that may prevent them from having a healthy viable pregnancy.

Prior to proceeding with ART all patients and partners should have completed a basic infertility evaluation. ART candidates who will be using their own eggs should be under 45 years of age and should have:

- No evidence of premature menopause
- At least one accessible ovary, and
- A normal uterus

Donor egg recipients should be under 48 years of age and have a normal uterus. All ART candidates should be in good health and have no medical conditions that would pose a serious health risk to themselves or the child they would carry.

GETTING STARTED

Before proceeding with any ART cycle, all patients and their partners must have completed the following:

Patient:

1. A uterine evaluation within one year of ART cycle (sonohysterography or hysterosalpingogram).
2. An egg reserve test (AMH or FSH) within one year of ART cycle.
3. Infectious disease panel within one year of ART cycle including: Hepatitis B, Hepatitis C, HIV, Chlamydia/Gonorrhea, Syphilis, Blood Type, and Rubella immunity.
4. IVF payment/insurance verification through our financial counselor.

Partner:

1. Infectious disease panel within one year of ART cycle including: Hepatitis B, Hepatitis C, HIV, Chlamydia/Gonorrhea, and Syphilis.
2. A semen analysis from an approved laboratory within the last year.
3. Optional freezing of back-up semen specimen.

Additionally, it is strongly recommended that all couples consider having the Counsyl Genetic Family Prep Screen completed to screen for genetic abnormalities. This is not required, but is available.

Once the above tests have been completed, you and your partner will be scheduled for an appointment with the IVF Nurse Coordinator to learn about the medications, injection techniques, and review the consent forms.

IN VITRO FERTILIZATION (IVF)

In Vitro Fertilization is the process by which the female oocyte (egg) is allowed to be fertilized by the male sperm outside the human body. Once fertilization has taken place, the resulting embryo is transferred into the uterus (Embryo Transfer-ET) in order for implantation to occur. This technology has enabled many couples, who thought that pregnancy was impossible, to have children.

The first child born by this procedure was Louise Brown in 1978. Since that time, there has been a dramatic increase in the use and refinement of both in vitro fertilization (IVF) and embryo transfer. To date, there have been several hundreds of thousands of children born to couples who, without IVF-ET, had little or no hope of bearing children. IVF is well suited for patients who have damaged or no fallopian tubes, but it is also being used at most centers around the country for other causes of infertility (i.e., endometriosis, low sperm count and unexplained infertility).

Following the successful fertilization of the eggs in the laboratory, the embryos are placed back into the woman's uterus roughly 3-5 days after fertilization. Based on the success rates in established clinics in the United States and abroad, live birth rate per egg retrieval for non-donor cycles, as averaged for all age groups, is 31.8% (*Clinical Summary Report, SART, 2013*).

IVF-ET consists of the following steps:

- A preparatory month using birth control pills, Lupron, Estrogen patches or a combination of these medications
- Ovarian stimulation using injectable gonadotropins specific to patient protocol
- Transvaginal ultrasound guided egg retrieval performed under anesthesia
- Fertilization of eggs in the laboratory using conventional insemination or Intracytoplasmic Sperm Injection (ICSI)
- Placement of fertilized eggs (embryos) into the uterus
- Luteal phase support with injectable progesterone
- Quantitative hCG pregnancy test

1. CONTROLLED OVARIAN STIMULATION AND MONITORING

Controlled Ovarian Stimulation (COS):

Controlled Ovarian Stimulation is the term used for the stimulation of the ovaries to produce multiple eggs (follicles). The drugs used are all in the form of injection. One of two types of drugs will be used to prevent the premature release of eggs. This allows greater control over the IVF cycle. Depending upon the stimulation protocol, Lupron[®] or Ganirelix[®]/Cetrotide[®] will be used to prevent the premature release of eggs. Your nurse will provide you with instruction on when to start this medication.

Medications called gonadotropins will be used to stimulate the ovaries to produce multiple eggs. There are several gonadotropin products on the market today (see page 20 for a listing of these medications). These drugs contain either the hormones FSH (Follicle Stimulating Hormone) and LH (Luteinizing Hormone) or FSH alone. These hormones are responsible for the production and maturation of eggs.

The last medication prior to egg retrieval is Human chorionic gonadotropin (hCG). This medication is used as a substitute for the midcycle hormonal surge which induces the final maturational changes in the eggs and prepares them for retrieval. hCG is administered when some of the follicles have reached appropriate size for retrieval (17-20mm).

Our protocols are modified to meet the needs of each individual patient. Approximately 5% of patients will not develop enough eggs for retrieval and will need to be cancelled.

Timing of Egg Retrieval:

The human egg is susceptible to fertilization for a short period of time. In IVF, it is important that the egg be at the right stage of development when it is exposed to sperm. Evidence of egg maturity is derived from both ultrasound measurements of follicle size and serum levels of estrogen (developing eggs produce estrogen). Once the eggs are at the appropriate size, hCG will be given to trigger the final development of the egg. This is the last step in the egg maturation process. The

hCG injection is given at night, and roughly 36 ½ hours after the injection the eggs are ready for retrieval and subsequent fertilization. Therefore, women undergoing ovulation induction for IVF will be followed in two special ways (ultrasound and estrogen measurements) to assess the development of the eggs in their ovaries.

Ultrasound:

A transvaginal ultrasound will give the physicians a visual description of the number of follicles developing, and the rate of development. Although one cannot visualize the egg by ultrasound, one can visualize the fluid filled sac (follicle) in which the egg is growing. The maturity of the egg correlates to the size of the follicle. Unfortunately, the ultrasound cannot always distinguish between a follicle containing an egg and a cyst; thus the estrogen level is very important in helping the physician distinguish between the two.

A baseline ultrasound will be required prior to starting any stimulation medications. This is typically performed on day 2 of the menstrual cycle. Ultrasounds will then be performed every 2-3 days until egg retrieval. Most women need an average of 3-4 ultrasounds with each cycle.

Estrogen Measurements:

Estrogen measurements will also be used to follow the growth of the eggs. Because the growing follicles produce estrogen, measurement of serum estrogen is used to guide adjustments in your medication dosage and to give an estimate regarding egg maturity. The test to measure estrogen in blood takes several hours to run; for this reason, blood is drawn in the early morning so that the results will be ready in the afternoon. Estrogen measurements will be obtained on the days that an ultrasound is scheduled. Both the ultrasound and estrogen level will be used to determine the dose of medication and/or the timing of the hCG injection.

2. EGG RETRIEVAL

The egg retrieval is performed in the Minor Procedure Suite via transvaginal ultrasound guided aspiration. This method of egg retrieval is accomplished by

inserting an ultrasound probe with a needle guide into the vagina. Anesthesia (conscious sedation) is required. Once the probe is lined up with the follicle (egg), the needle is advanced into the follicle and the fluid is removed. The probe is then redirected and the same method is employed until all eggs have been removed.

After the eggs are collected, they are taken to the lab adjoining the procedure room. While you are recovering from the procedure, the lab personnel will be identifying the eggs and preparing them for fertilization. You will receive an egg count at conclusion of the procedure.

3. FERTILIZATION

The contents of each follicle that is aspirated will be examined for an egg. Each egg will be graded as to its state of maturity and placed in a separate dish. The dish is then transferred to the incubator which provides an environment suitable for fertilization and development of an embryo. On the day of egg retrieval, a semen sample will be obtained. If conventional insemination is indicated, washed sperm will be placed alongside the egg in the dish. If intracytoplasmic sperm injection (ICSI) is used, a single sperm will be injected into each egg. This technique is best suited when the sperm count or motility is low. Depending on the quality of the sperm and eggs, one can expect 50%-70% of the eggs will fertilize. Cell division of the fertilized egg will begin about 24-36 hours after retrieval. The embryologist will evaluate the embryo development and provide updates periodically.

4. EMBRYO TRANSFER

Embryo(s) will be ready for transfer on Day 3 or 5 following egg retrieval. This decision will be based on embryo quality and development. The embryo transfer is an in-office procedure that does not require anesthesia. Prior to the procedure, the embryologist will meet with each couple to discuss the number of embryos to be transferred, quality and grading. Please refer to page 26 for detailed instruction for embryo transfer day.

5. LUTEAL PHASE SUPPORT

Progesterone, which is produced by the ovary after ovulation, is important for fostering early conditions suitable for implantation of an embryo. Progesterone levels in IVF cycles are usually more than adequate because of the stimulation of the ovaries involved in the first part of the cycle. However, since the process of egg retrieval removes some of the cells that are responsible for making progesterone, it is important to supplement with progesterone following the egg retrieval. This supplementation will be in the form of progesterone injections. This medication will increase the levels of progesterone during the time of early pregnancy. Patients will stay on progesterone until the results of their pregnancy test are known. If a pregnancy has occurred, the progesterone will be continued for an additional 4 weeks.

6. PREGNANCY TEST

Pregnancy tests are done 8-10 days following the embryo transfer. This blood level will be drawn in the morning and results will be called to the patient in the late afternoon of the same day. If this day falls on a weekend, the blood test will take place on the following business day.

RISKS ASSOCIATED WITH IVF

Ovarian Hyper-Stimulation Syndrome:

A rare complication of IVF is Ovarian Hyper-Stimulation Syndrome (OHSS). OHSS can occur when too many eggs are being developed in combination with a very high estrogen level. When eggs are aspirated from the ovary, hyper-stimulation is rare. In the rare event this does occur, symptoms may include pain, fluid shift into the abdomen, and alterations in circulation.

Multiple Gestations:

When more than one embryo is returned to the uterus there is a risk of a multiple gestation. If pregnancy occurs, there is roughly a 25% chance of having twins with IVF and a 3%-5% chance of higher order multiples. You will be counseled about the number of embryos to transfer. When possible, single embryo transfers are recommended to avoid multiple gestation. Some conditions (advanced maternal age) may necessitate multiple embryos transferred to achieve a singleton pregnancy.

Egg Retrieval:

While rare, the risks of vaginal ultrasound retrieval include the possibility of bleeding, injury to internal organs, or infection which might require antibiotic treatment. Although adverse reactions are very rare, you will be monitored closely during and following the retrieval. There may be some discomfort with the procedure; however, you will be given IV sedation.

Tubal Pregnancy:

While rare, all ART procedures can result in an ectopic (tubal pregnancy). The 2011 rate of tubal pregnancy per embryo transfer was 1.6%. All women with a positive pregnancy test will be followed carefully to facilitate early diagnosis of this condition.

Additional Concerns:

All couples have a 2%-5% risk of having a child with a birth defect. For years, data obtained from IVF centers across this country have not shown an increase in birth defects in children conceived from IVF techniques. More recent studies have shown around 4% of children conceived through IVF have some birth defect. Other factors can contribute to birth defects including advanced age of the mother and chromosomal abnormalities in the couple. IVF and associated techniques may also increase this risk; however, at this time there is limited evidence as to the role IVF has in increasing risk.

Roughly 18% of all pregnancies will result in a miscarriage, and 1% of all pregnancies will end in a tubal pregnancy. While miscarriages often require no intervention, they occasionally need to be managed with a D&C (Dilation and Curettage). Tubal pregnancies can be life threatening if not diagnosed early and must be removed, usually by laparoscopy.

There has been some concern regarding the use of ovulation induction agents and the development of ovarian cancer. More recent studies, however, have refuted the initial claims about such a link.

Additional ART Procedures

EMBRYO CRYOPRESERVATION

In the early to mid 1990's the technique of freezing embryos was developed and refined. Today, embryo cryopreservation is standard practice in many IVF centers. In embryo cryopreservation, eggs are fertilized with sperm and a portion of the resulting embryos are transferred to the patient. The remaining embryos are frozen and transferred at a later date. It is recommended that only 1-2 embryos should be transferred at one time; therefore, any embryos meeting the freezing criteria will be cryopreserved for future use. If the couple does not become pregnant, or they wish to have another child, they can return to have the frozen embryos thawed and transferred without having to undergo ovarian stimulation and egg retrieval. This technology has increased the pregnancy rate for IVF by increasing the number of embryo transfers from one egg retrieval. The national live birth rate per transfer of thawed embryos is 40.1% (*Clinical Summary Report, SART 2013*).

Although the delivery rate from embryo transfer with frozen/thawed embryos is lower, it has steadily increased over the years as laboratory techniques have been refined. Frozen embryos are thought to be viable indefinitely once they are frozen. The steps of embryo transfer with cryopreserved embryos are:

- 1) Preparation of the endometrium (lining of the uterus) with estrogen beginning day 2 of period
- 2) Ultrasound and bloodwork after approximately 2 weeks of estrogen exposure
- 3) Daily progesterone injections to be started on a specified date
- 4) Thawing of embryos and transfer to the uterus after six days of progesterone therapy

Although embryo cryopreservation is a good option for many couples, not every patient will have embryos to freeze. The decision to freeze remaining embryos will be made on day 5 or 6 of embryo development, and will be determined by the embryologist.

MICROMANIPULATION

Advances in microscopic equipment and knowledge about eggs, sperm and embryos have led to the development of new techniques in ART.

Micromanipulation refers to the handling and manipulation of individual eggs, sperm, or embryos in an effort to improve fertilization and/or pregnancy rates. These techniques require specialized equipment and personnel. Currently the most common micromanipulation techniques used are **Intracytoplasmic Sperm Injection (ICSI)** and **Assisted Hatching**. **ICSI** is used to assist fertilization in cases of severe male factor infertility. **Assisted Hatching** is used to help the inner cell mass of the embryo “hatch” from the zona pellucida (outer shell). In addition, our facility also offers single gene disorder screening (**Pre-Implantation Genetic Diagnosis-PGD**), and chromosome abnormality screening (**Pre-Implantation Genetic Screening-PGS**). **PGD** is available for couples who have a genetic disorder that they do not wish to pass on to an offspring or which impairs their ability to maintain a pregnancy. **PGS** is available for couples who wish to screen for chromosomal normalcy.

Intracytoplasmic Sperm Injection (ICSI)

The ICSI technique was developed in the early 1990’s to treat cases of severe male factor infertility. This technique involves injecting a single sperm into the interior (cytoplasm) of an egg. ICSI is not a guarantee of fertilization; however this intervention can overcome poor semen parameters.

Candidates for ICSI may include patients with very low sperm counts, poor motility, and/or abnormal morphology. This technique is also used in couples with a history of failed fertilization with conventional insemination. ICSI may also be used to achieve fertilization using surgically extracted sperm from patients with anatomic or surgical conditions (such as vasectomy) that prevent sperm from entering the ejaculate.

Risks Associated with ICSI

Recent evidence suggests that some forms of severe male factor infertility are genetic and may be passed on to male offspring through the ICSI procedure. In some studies, the incidence of congenital abnormalities (birth defects) following ICSI appears to 1%-2% higher than that of the general population.

Some risks associated with ICSI include: possible genetic consequences of selecting an abnormal sperm for injection, degeneration of the egg caused by sperm injection, decreased fertilization rate, poor or arrested embryo development, and reduced chance of a successful pregnancy outcome. There is no guarantee that ICSI will result in either fertilization or pregnancy.

The alternatives to ICSI for treatment of severe male factor infertility are limited. One option is the use of donor sperm. Using donor sperm normalizes the success of conventional IVF-ET in couples with severe male factor infertility. In cases where male factor is the only diagnosis, pregnancies with donor sperm can be achieved through timed intrauterine insemination, a treatment far less expensive and complicated than IVF-ET.

Assisted Hatching

Assisted Hatching is a process wherein a special solution or a low-energy laser beam is used to dissolve the thick coating around the embryo. There is a small risk of damage to the embryos from the procedure. It is not clear which patients are the best candidates for assisted hatching. Currently, the laboratory uses Assisted Hatching on all Day 3 embryo transfers and all Frozen Embryo Transfers (non PGS/PGD embryos). In order to perform Assisted Hatching patients must sign a separate consent.

Pre-Implantation Genetic Diagnosis (PGD)

Pre-Implantation Genetic Diagnosis (PGD) can be used in conjunction with IVF to screen embryos for genetic abnormalities. This procedure involves taking a biopsy from the trophectoderm (outer shell) of a Day 5 embryo (Blastocyst) and

analyzing the genetic material (DNA) for abnormalities. PGD is offered to patients who are carriers of single gene disorders (diseases that can be traced to a specific location on a gene).

Couples who wish to proceed with PGD testing will be referred to Genesis Genetics for registration and probe creation. You will be required to submit a cheek swab and DNA sample, which will be used to build a probe specifically designed for your family. When the probe is complete, the biopsied cells are analyzed to determine embryos that have inherited the disease and those embryos that are free from the disease.

Pre-Implantation Genetic Screening (PGS)

Pre-Implantation Genetic Screening (PGS) is an IVF procedure designed to examine your embryos for chromosomal abnormalities. Screening can potentially benefit those who present with the majority of IVF cases, particularly advanced maternal age couples and families who suffer with recurrent pregnancy loss. This procedure involves taking a biopsy from the trophectoderm (outer shell) of a Day 5 embryo (Blastocyst) and analyzing the genetic material chromosomal for abnormalities. Chromosomal abnormalities can result in aneuploidy (embryos having the wrong number of chromosomes), or translocations. PGS aims at improving pregnancy and live birth rates by allowing your physician to transfer only those embryos that are chromosomally normal.

Risks Associated with PGD and PGS

As in any conception, there is a risk of birth defects in children born following PGD/PGS testing. There is also the risk of a false negative result, which would lead to embryos being transferred that carry the disease in question. Additionally, it is possible that the test will find that there are no embryos suitable for transfer.

OOCYTE DONATION

For some women pregnancy with their own eggs is impossible. A few women carry a genetic defect which should not be passed on to their offspring; other women may not be able to produce eggs. This may happen due to premature failure of the ovaries (early menopause), surgical removal of the ovaries, or failure of the ovaries to respond adequately to ovarian stimulation. Advancing age also affects and contributes to lower pregnancy rates and higher fetal defects in women over the age of 35.

Anonymous Egg Donation offers the opportunity for women to experience pregnancy and expand their families. Through third party anonymous Egg Donor Banks, prospective donors and intended parents are matched as closely as possible through selective profiles. The recipient couple will not have access to identifying information of their donor and conversely the donor will not have access to the identity of the couple receiving her eggs. The live birth rate per transfer is roughly 56.1 % (*Clinical Summary Report; SART, 2013*).

Steps involved in IVF with donor eggs include:

- 1) Identify donor agency and elect anonymous donor
- 2) Physical screening of the donor including reproductive profile to ensure appropriate response to stimulation
- 3) Legal agreements/contract, consent forms, psychological screening, and FDA infectious disease screening
- 4) Ovulation induction of the donor using gonadotropins
- 5) Synchronized stimulation of the uterine lining of the recipient using Estrogen and Progesterone
- 6) Ultrasound guided egg retrieval of the donor
- 7) Fertilization of the donor's eggs with designated sperm source
- 8) Transfer of the resulting embryos to the recipient's uterus

It is also important to consider the psychological aspects of using donated eggs. Many couples may have fears that a child conceived with donated eggs or sperm may not look like them or they may fear that they will not be able to bond to the

child as they would a child conceived with their own eggs or sperm. Although these concerns are very common, they do need to be dealt with before proceeding with a Donor IVF cycle. If you are considering the use of donor eggs or sperm, you may be required to meet with a psychologist to discuss this option in detail and explore the psychological issues regarding donor gametes.

INSTRUCTIONS FOR SEMEN SPECIMENS

A semen analysis is required in preparation for IVF. Results will determine the method of fertilization used in IVF. If your partner is providing a fresh sample, this will be collected on egg retrieval day.

Below are instructions you should follow for each collection:

IT IS IMPORTANT THAT YOU PROVIDE THE SPECIMEN AT THE DESIGNATED TIME. FAILURE TO DO SO MAY REQUIRE POSTPONEMENT OF YOUR IVF CYCLE.

1. Please abstain from any ejaculation 2-5 days prior to your appointment. Abstinence for a longer or shorter period of time may affect the results. The preferred method of collection is by masturbation. Do not use a condom, and use only approved lubrication (Preseed) while obtaining the specimen. Most condoms contain a spermicide that will adversely affect semen quality.
2. The specimen may be collected at home or in the clinic collection room. If the specimen is collected at home, it must be in the office no more than one hour after collection. Specimens must be collected in a sterile container with a screw on lid. Keep the specimen between room and body temperature (70-98.6 degrees). All containers must be labeled with your name, partner's name and time of collection.
3. Please bring a valid and current form of picture identification and insurance card with you at the time of your appointment for verification.

DAILY INSTRUCTIONS FOR YOUR CYCLE

The following pages contain information and instructions for you to follow in relation to your IVF cycle. You will find it helpful to review this material each time you enter a new phase of your cycle. Please refer to your specific protocol to see which information is pertinent to you.

You may also find it helpful to keep a calendar of clinic appointments. Please bring your workbook to your appointments so that we can make notes or changes if necessary.

MEDICATIONS

Common Name	Actual Name	Purpose
Ganirelix® Cetrotide®	GnRH antagonist	To prevent spontaneous release of eggs
Lupron®	GnRH agonist	Ovarian suppression/prevent spontaneous release of eggs
Follistim® Gonal-F®	Gonadotropins (FSH only)	Stimulate ovaries to develop multiple eggs
Menopur®	Gonadotropins (FSH and LH)	Stimulate ovaries to develop multiple eggs
Novarel® Pregnyl®	hCG	Final injection before egg retrieval, used to mature eggs

In addition to the information you will receive from us regarding your medications you may also access specific information on-line at the following website: www.freedommedteach.com

You will be required to attend a Medication Injection Teach class. Classes are offered Tuesdays and Thursdays at 10am by appointment only.

GONADOTROPINS (FSH, FSH/LH)

There are a variety of gonadotropins available for ovarian stimulation. You will be prescribed one or a combination of the following: Follistim[®], Gonal-F[®], and Menopur[®]. Gonadotropins are given to stimulate the ovaries to produce several follicles in one cycle. This allows the providers to retrieve more eggs and thus ensures a greater chance of fertilization.

Side Effects:

Side effects associated with these medications include injection site reactions and ovarian hyper-stimulation. Other reported side effects include dizziness, nausea, headaches, irritability and hot flashes. These, however, are thought to be associated with the increase in estrogen levels from the stimulated follicles.

Risks:

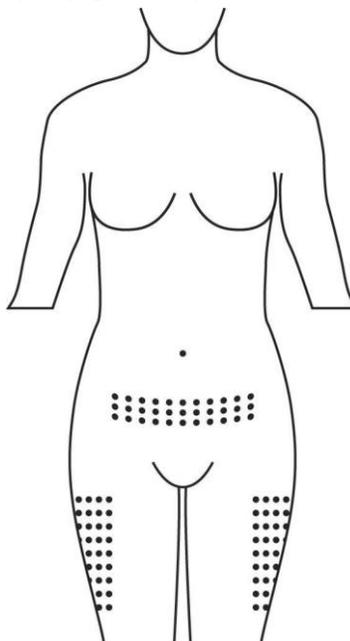
Hyper-stimulation of the ovaries is a potential risk when taking ovulation induction agents. Hyperstimulation occurs when the ovaries become enlarged. In mild to moderate cases of hyperstimulation, a person may experience abdominal distension and/or abdominal pain. Approximately 20% of patients will experience mild hyperstimulation. Symptoms usually resolve with the onset of menses, but in the case of pregnancy may continue for several weeks.

In severe hyper-stimulation (less than 1% of patients in IVF programs), ovarian enlargement is accompanied by accumulation of fluid in the abdomen, nausea, vomiting, weight gain and a decrease in urine output. Women who experience severe hyperstimulation require hospitalization.

If you notice any of the following symptoms, please call the IVF office immediately: weight gain of over 5 pounds from your baseline weight, a decrease in your urine output, severe abdominal pain, dizziness upon standing, nausea or other discomfort which you find concerning.

Subcutaneous Injections (Lupron® /Follistim®/Gonal-F®/ Menopur®, hCG (Novarel®, Pregnyl®):

1. Select the site for administration.
2. Gently wipe the site with alcohol pad.
3. Tightly hold the medication-filled syringe and remove cap if necessary, being careful not to touch needle.
4. Hold syringe with needle pointing up and gently tap the syringe to move any air bubbles to the top of syringe.
5. If there is air in the top of the syringe, gently push the plunger up to remove air. Stop pushing the plunger when you no longer see air in the syringe.
6. Hold syringe with your dominant hand close to the base of the needle (hold syringe like a dart).
7. With the other hand, gently grasp a fold of skin at the injection site between your thumb and index finger.
8. Quickly insert needle into the fold of the skin all the way to the base of the needle.
9. Slowly push plunger to inject all of the contents in the syringe.
10. Withdraw needle and place in sharps container.
11. If there is any bleeding at the injection site, place a dry cotton ball or bandage over site and apply gentle pressure for 1-5 minutes.



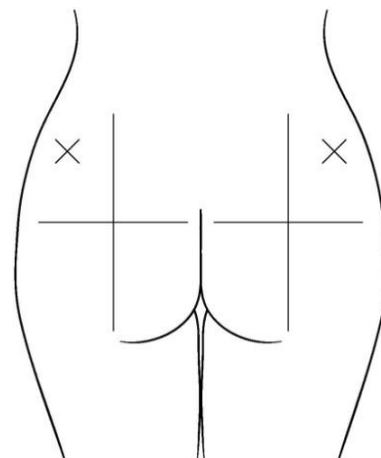
Intramuscular Injections (Progesterone):

Drawing up the medication:

1. Wash your hands
2. Flip off plastic lid or metal tab on top of vial. Wipe the rubber stopper with an alcohol swab. This will be a multiuse vial with enough medication for 10 days. DO NOT REFRIGERATE
3. Use a 3 cc syringe with an 18-gauge, 1 ½ inch needle
4. Insert needle into the rubber stopper. Keep needle in the vial, turn vial upside down, keeping the needle below the fluid level and pull back on plunger, withdrawing 1 cc of liquid (liquid fills slowly). Flick syringe with finger to force air to surface, then push up plunger to expel air.
5. After drawing up the medication, change to the 22 gauge 1 ½ inch needle for injection.
6. Follow instructions for intramuscular injection.

Injecting the medication:

1. Cleanse the injection site with alcohol. Wait a few seconds until alcohol has dried on skin. Remove cap from needle.
2. Spread the skin, and insert the needle at a 90-degree angle into the skin as far as it will go.
3. Anchor the syringe with your free hand. Pull back slightly on the plunger; if you see blood return, remove the needle and re-inject in an alternate site.
4. If there is no blood return, inject medication slowly.
5. Withdraw the needle at the same angle at which it was inserted. Apply pressure at the injection site with gauze or tissue.
6. Dispose of used needle and syringes carefully in an approved sharps container.
7. Alternate sides with each daily injection.
8. Massage the injection site and use a heating pad for 20 minutes after the injection to help with absorption into the muscle.



PRE-RETRIEVAL INSTRUCTIONS

You will be scheduled for egg retrieval approximately 36 1/2 hours after your injection of hCG. Egg retrieval will take place either in the morning or early afternoon. You will go to the Minor Surgical Procedure Suite located next door to our office in the Medical Plaza-Miller building. You will be told by our staff at what time to report to the Surgical Suite. Below are instructions to follow prior to your retrieval.

The night before egg retrieval:

1. Eat a good supper and have a late night snack
2. Abstain from intercourse
3. Do not eat or drink anything after midnight.

The morning of egg retrieval:

1. Remove any make-up, hair pins, jewelry, or contact lenses
2. No perfume (deodorant is ok)
3. Do not eat or drink anything
4. Arrive in the Minor Procedure Suite at the designated time.

THE DAY OF EGG RETRIEVAL

On the day of egg retrieval you will be asked to report to the Minor Procedure Suite located on the second floor of Medical Plaza-Miller. Personnel from the procedure suite will meet you and direct you to the waiting area. You will be given a place to store your clothing. The nurse anesthetist will talk with you and discuss your sedation at that time. An IV will also be placed in your arm, and pre-operative vital signs will be taken. The lab will tell your partner where and when to go to collect his semen specimen, if using fresh semen.

Once all the pre-operative work has been completed, you will be wheeled to the procedure room and transferred to the procedure table. The nurse anesthetist will begin to administer your sedation. You will be breathing on your own throughout the procedure, and may require supplemental oxygen. You will be draped with sterile sheets and towels. The doctor will then clean your vagina with a sterile solution.

Once the vagina has been thoroughly cleaned, the doctor will insert the vaginal ultrasound probe. Your doctor will then proceed to aspirate the follicles (fluid filled sacs containing the eggs). Lab personnel will be present for identification of the eggs. After all the follicles have been aspirated, the nurse anesthetist will begin to withdraw your sedation.

You will then be transferred to the recovery room where you will stay for approximately one hour. **You must be accompanied by a partner or friend in order to be discharged.** Your physician will meet with you before you are discharged to review your post-operative instructions and precautions.

After Your Egg Retrieval

Following the egg retrieval, you may experience some abdominal soreness, vaginal spotting, nausea and/or vomiting. These symptoms should resolve within a couple of days. **However, you should call the doctor if you experience excessive bleeding, difficulty breathing, severe pain, dizziness, or develop a fever. You may take Tylenol as needed for pain relief. DO NOT TAKE Ibuprofen/Aleve/Motrin.**

EMBRYO TRANSFER

The embryologist will call the day after your egg retrieval to discuss your fertilization results. Embryo transfer will take place either 3 or 5 days after egg retrieval. This decision will be determined by the lab director and your physician.

The Embryo Transfer does not require anesthesia. The procedure will be performed under ultrasound guidance with a full bladder. One hour before the procedure you should urinate to empty the bladder; then drink 24 ounces of fluids within 15-20 minutes to re-fill your bladder.

Prior to transfer, you will meet with the Embryologist to discuss how many embryos will be placed into the uterus. You will be escorted to the procedure room, asked to undress from the waist down, and draped with a sheet. The transfer will be performed using sterile procedure. The physician will place a speculum in the vagina. The vagina and cervix will be thoroughly cleansed before transferring the embryo(s). An abdominal probe will be placed on the abdomen so that the uterus can be visualized. The embryo(s) will be transferred into your uterine cavity via a catheter guided through your cervix.

You may feel some mild cramping during the transfer; however this should resolve once the catheter is removed. After the embryo(s) is transferred you will be asked to rest on the exam table for approximately 10-15 minutes.

Implantation Support

After the transfer, there are several things you can do to help the embryo have the best possible chance of implanting. The first is to continue medications that support the uterine lining and help to maintain a pregnancy. These medications (progesterone injections, and estrogen pills and patches for FET patients) will be taken until the pregnancy test. If your pregnancy test is positive, you will continue all medications until 8-10 weeks gestation. It is recommended to continue prenatal vitamins and baby aspirin.

Additionally, you'll be asked to do "couch rest" after the embryo transfer - take the day off, put your feet up and rest as much as possible. After the first 24 hours, patients should continue to take it easy for an additional three or four days. You can go back to work and lead your normal life, but strenuous exercise,

chores, and even sexual relations should be avoided. Anything that causes uterine contractions could affect the implantation process.

Pregnancy Test

Your quantitative hCG “pregnancy test” will be scheduled 8-10 days after your day 5 transfer, or 10-12 days after your day 3 transfer. Please note that these tests are not done on the weekends.

As tempting as it is, fertility patients are advised not to use home pregnancy tests. Home pregnancy tests can render false results for fertility patients, either negative or positive. A false positive can result because hCG is given to “trigger” ovulation and may remain in the blood and a home pregnancy test cannot determine the difference between the two. A false negative might occur because a low level of hCG may be undetectable in a urine test despite a pregnancy starting.

When the Test is Positive

If your pregnancy test is positive, your doctor or nurse will tell you the hCG level that your test showed. The test result is stated as a number that indicates the level of hCG found in the blood. This number will increase fairly rapidly in healthy pregnancies, so multiple pregnancy tests will be ordered over the next several days to confirm the pregnancy is developing normally.

A blood hCG level over 50mIU/mL is a good first result but many, many ongoing pregnancies start out with an hCG level below that number. You'll be asked to repeat the test in 2 to 4 days. The goal is to watch the trend of your hCG to confirm that it is rising appropriately.

If both blood tests indicate a healthy pregnancy, then a vaginal ultrasound will be scheduled at the 6 week mark of the pregnancy. At that time, your doctor will be looking for a gestational sac to confirm the pregnancy. Your subsequent ultrasound will be scheduled at the 8 week mark of pregnancy, at which point we expect to see a fetal heartbeat.

Most patients will continue to take hormone medications throughout this 8-10 week period to support the developing pregnancy. At the end of 8-10 weeks, you will be released back to your regular OB/GYN to begin normal prenatal care.

If the Results are Negative

If you get a negative result on your pregnancy test, it's very disappointing. It's important to remember, though, that you have a treatment plan with options for trying again. We will support you in every way we can.

We will start by instructing you to stop your medications and schedule a consultation with your doctor. At that time, you'll discuss what happened during the cycle, how you want to proceed and any changes you might make to your protocol.

Some patients may start a new IVF cycle or FET cycle on their next menstrual cycle while others may have to wait a month or two longer. Patients should remember that not everyone is successful on their first cycle but that doesn't mean that success in subsequent attempts is impossible.

PAYMENT POLICY

IVF can be an expensive endeavor especially if you do not have insurance coverage. We make every effort to keep the IVF and associated procedures affordable options for infertility patients.

It has been the policy of Wake Forest University Physicians and North Carolina Baptist Hospital to require payment of elective procedures and therapies prior to the initiation of treatment. If you have insurance coverage for IVF, you may be asked to pay the portion your insurance does not cover before initiating treatment.

All couples are asked to call Patty Joyner, the Financial Counselor, to discuss payment of your IVF cycle. If you do not have insurance coverage for IVF, you will be asked to pay the cost of the cycle prior to beginning the stimulation medications. Patty Joyner will assist you with this process.

IMPORTANT PHONE NUMBERS

<p>The Center for Reproductive Medicine</p> <ul style="list-style-type: none"> • Office hours are 8:00am-4:30pm • Telephone hours are 8:30am-3:00pm, closed 12noon-1:00pm for lunch 	716-6476
<p>Sarah Berga, M.D. Erika Johnston-MacAnanny, M.D. Bonnie Patel, M.D.</p>	716-6476
ART/Andrology Lab	716-3677
<p>Emergencies: after 4:00 p.m., weekends, and holidays (have the operator page the doctor on call for The Center for Reproductive Medicine)</p>	716-2011
Roxanne Kennedy, RN, BSN, Infertility Coordinator	716-3778
Lauren Edington, CMA, Infertility Coordinator	716-6198
Kim Broome, RN, MSN Clinic Coordinator	716-2451
<p>Pharmacies:</p> <p style="padding-left: 40px;">Freedom Drugs</p> <p style="padding-left: 40px;">NCBH Outpatient Hospital Pharmacy</p> <p style="padding-left: 40px;">South Miami Pharmacy (SMP)</p>	<p>800-660-4283</p> <p>336-716-3363</p> <p>305-740-9696</p>
Financial Counselor (Patty Joyner)	716-1269