Boston IVF

OVULATION INDUCTION & INTRAUTERINE INSEMINATION TREATMENT:

What every patient should know

BOSTON IVF-The Boston Center
One Brookline Place
Brookline, MA 02445
Tel. (617) 735-9000

BOSTON IVF-TheSouth Shore Center
2300 Crown Colony Drive
Quincy, MA 02169
Tel. (617) 793-1100

BOSTON IVF-The Waltham Center
130 Second Avenue
Waltham, MA 02451
Tel. (781) 434-6500

www.bostonivf.com

TABLE OF CONTENTS

This guide will provide you with an understanding of the treatment that has been recommended by your physician. The information in this guide adds to the discussions you have had with your Boston IVF physician. Boston IVF wishes you quick and positive results.

BEFORE STARTING TREATMENT

There are several steps that must be completed before the treatment can be started.

- **Medical Evaluation**
  Prior to starting treatment, all testing ordered by the physician must be completed. At the consultation the physician will review the test results and discuss the treatment in detail.

- **Visit our website** *(www.bostonivf.com)*
  Our website has a number of documents that will help you get started. Go to our website (www.bostonivf.com) and click the "for patients" button—type in the *username* **bostonivf** and the *password* **patient.** The following documents can be printed off- cycle calendar and consent forms.

- **Orientation & Injection Teaching**
  Please go to one of the web sites below to learn more about the injections:

  - *www.villagepharmacy.com* -- click on "Video injection lessons" then enter the user id code **"Village1"** and password **"fertility"** once you have entered please select the medication video that applies to you.

  - *www.freedommedteach.com*-- you will need your prescription number in order to view the injection videos, this can be obtained on your prescription that has been filled by Freedom Drug.

  Please contact patient educational services at **781-434-6524** several weeks before you plan to start treatment to learn more about the treatment and the injections.

- **Consent Form**
  The consent form can be downloaded from our website. A consent form must be signed and witnessed by one of our clinical staff prior to the initiation of treatment. The form can be downloaded from our website. Please call your clinical assistant to arrange signing of the consent form(s) if it has not been signed already.

- **Insurance Authorization**
  Prior to initiation of the treatment, insurance approval must be in place. We will work with you to get approval for the treatment. It may take several weeks to get the final approval from your insurance company. For your convenience we have produced a separate booklet that describes the

insurance process in Massachusetts. Information in the booklet may prove useful to patients who live in other states as well. The booklet is available on-line at www.bostonivf.com/documents.

GETTING READY FOR A PREGNANCY

At Boston IVF, our goal is to not only help you achieve a pregnancy, but to have a healthy pregnancy, as well. There are certain things that you can do to achieve this goal.

Smoking
If you smoke, you must stop! The bad effects of smoking on general health are well known (e.g., heart disease, cancer and chronic lung disease). Women who smoke during pregnancy are at increased risk of complications. Men and women who smoke have decreased fertility. If you can't stop smoking on your own then you should contact your primary care physician.

Alcohol
Alcohol intake can impair male and female fertility. Women trying to conceive should completely avoid alcohol or limit use to the first 2 weeks of the menstrual cycle. During pregnancy alcohol is absolutely contraindicated.

Caffeine Intake
Caffeine's affect on fertility has been the subject of controversy. Several studies have concluded that caffeine decreases the chance of conceiving. However; a cause and effect relationship between caffeine intake and fertility has not been absolutely confirmed. Nevertheless, it is reasonable to suggest that women discontinue or at least limit their intake to one caffeinated beverage a day.

Drug Use
The use of recreational drugs is contraindicated while attempting to conceive and during pregnancy. Some drugs, such as marijuana, may decrease sperm concentration and testosterone hormone production in men.

Diet
Ingestion of some fish, which contain higher amounts of mercury, can affect the development of the nervous system of a fetus. During the treatment and after pregnancy is established you should avoid eating these fish- shark, swordfish, king mackerel, tilefish and canned tuna fish. You should limit the intake of all other fish to 12 oz. per week.

Vitamin Supplementation
Folic acid supplementation can significantly reduce the occurrence of neural tube defects in infants. Neural tube defects are abnormal developments of the spine and skull. All women should take at least 0.4 mg of supplemental folic acid per day. This can be accomplished either through dietary supplementation or by taking an over-the-counter multivitamin (or prenatal vitamin).

Excessive intake of vitamin A increases the chance of congenital anomalies. Prenatal vitamins and over-the-counter multivitamins usually contain 5,000-8,000 IU of vitamin A, which is a safe dose. However, your daily intake should not exceed 8,000 IU.

Routine medical care
You should have a yearly visit with you primary care physician or gynecologist for a routine exam. A pap smear must be recent and performed within the past year. A baseline mammogram to screen for breast cancer should be performed between ages 35-40 and after age 40 the mammogram should be done every other year. If the Pap smear is not up-to-date or you need to schedule a mammogram, you should contact your gynecologist or primary care physician.

Exercise
The benefits of exercise on general health and mental well being are well established. Further, moderate exercise during pregnancy is also beneficial. If you were already in an exercise program, we would encourage you to continue. However, the medications used to stimulate the ovaries can cause ovarian cyst formation and ovarian enlargement. Therefore, we would advise you to avoid exercise activities that result in a lot of vertical movement (i.e., running, step aerobics). Other exercise activities such as swimming, bicycle riding, walking and using the treadmill or elliptical are acceptable.

Medication Use
All non-fertility medications that have been prescribed should be discussed with your physician. It is also important that your physician who originally prescribed these medications be made aware that you are attempting pregnancy. You should avoid taking aspirin and aspirin-like compounds (such as Advil®, Aleve®, Ibuprofen, Motrin®) around mid-cycle, since these medications can interfere with ovulation. Tylenol® is a suitable alternative.

INSURANCE COVERAGE

Prior to treatment it is essential that you determine the extent of insurance coverage that is in place. To understand this better please read below:

- **Speak with one our financial counselors**—we have experienced financial counselors who will investigate the extent and any limitations in your insurance coverage. Different forms of treatment require different levels of insurance company authorization.

- **It can take some time-** your insurance company may require specific information or testing prior to authorizing treatment. This is in addition to and separate from any referrals that are issued by your primary care physician. Please realize that obtaining insurance company authorization takes time sometimes up to 2 weeks. A little pre-planning on your part can help avoid frustrating delays in treatment.

- **If you change your insurance plan--** If you are changing insurance plans it is critical that you notify our financial counselors immediately. Sometimes a change in insurance policies will delay initiation of treatment. Fortunately, you can minimize and often avoid these delays entirely by giving a copy of your new insurance card (both sides) to our financial counselors and your Boston IVF doctor's secretary.

- **Go to our website to learn more** A more comprehensive discussion about insurance and fertility treatment can be found in the Boston IVF publication *"Guide to Infertility Insurance Coverage"* available on-line at www.bostonivf.com. Go to our website and click on “for Patients” button on the top right hand side. Log in with the username “*bostonivf*” and password “*patient*”.

COUNSELING AND SUPPORT: WHEN AND WHERE TO FIND IT

Few situations in life are as challenging, demanding and stressful as infertility and its treatment. Patients often express a sense of loss of control over their lives when pregnancy does not come quickly. Multiple tests and office visits can compound the anxiety for some patients.

Boston IVF offers individual and couples counseling with professionals who specialize in fertility issues. Our goal is to help patient's sort out their feelings, identify coping strategies and to feel better about themselves during their fertility treatment.

OUR COUNSELING STAFF

Jeanne Ungerleider, LICSW 617-739-4791 ext. 201
Terry Chen Rothchild, LICSW 617-964-6626
Lynn Nichols, LICSW 978-369-2390

THE DOMAR CENTER FOR MIND/BODY HEALTH

The Domar Center at Boston IVF in Waltham offers multiple resources for patients. These services include mind/body groups, acupuncture (offered seven days per week), massage, nutritional counseling, individual and couples cognitive behavior therapy, and yoga classes.

Recent research has shown that the more distressed one is before and during infertility treatment, the less likely it will be for you to get pregnant. Thus, all patients are strongly advised to make an appointment for a *mind/body consultation*. This 50 minute visit with a psychologist is designed to assess your current physical and psychological health, as well as your symptoms, and the goal of the session is to come up with a treatment plan designed entirely for you. This session is billed to your insurance company under your mental health benefits.

Research has also shown that:

- participants in mind/body groups have significantly higher pregnancy rates than women who do not participate
- acupuncture is associated with significant increases in pregnancy rates
- women who have a body mass index (BMI) which is too low or too high have lower pregnancy rates than women whose BMI is in the normal range

All Domar Center services are offered in Waltham; acupuncture is also offered in Brookline and Quincy. For more information on the Domar Center, please call 781-434-6578 or see www.domarcenter.com.

SUPPORT GROUPS

The American Fertility Association
666 Fifth Avenue, Suite 278
New York, NY 10103
Tel: (888) 917-3777
www.theafa.org

Resolve of the Bay State
P.O. Box 541553
Waltham MA 02454-1553
Tel: 781-647-1614
www.resolveofthebaystate.org

MEDICATIONS USED FOR OVARIAN STIMULATION

Medications are prescribed to improve the quality of the ovulation and to increase the number of eggs that are released at the time of ovulation. To get a better understanding as to how these medications work it is worthwhile to provide you with a quick review what happens naturally.

The eggs are present in the ovaries within fluid-filled cysts called follicles. During a woman's menstrual cycle, usually one mature follicle develops, which results in the ovulation of a single egg. Several hormones including follicle stimulating hormone (FSH) and luteinizing hormone (LH) influence the growth of the ovarian follicle. These hormones are produced by the pituitary gland, which is located at the base of the brain. FSH is the main hormone that stimulates the growth of the follicle, which produces an estrogen hormone called *estradiol*. When the follicle is mature, a large amount of LH is released by the pituitary gland. This surge of LH helps to mature the egg and leads to ovulation 36-40 hours after its initiation.

There are several types of medications that can be used to stimulate the ovaries which are described below.

Oral Medications

Clomiphene Citrate (Clomid®, Serophene®)
Clomiphene citrate is a synthetic hormone that is taken orally for a period of five days and causes the release of FSH and LH, which stimulate the development of follicles. It is considered a mild stimulant of the ovaries.

Common side effects include- changes in mood, hot flashes, headaches, visual changes, pain with ovulation.

Injectable Medications

Gonadotropins - gonadotropins are injectable medications commonly prescribed to stimulate the ovaries of women undergoing IUI treatment. All of these medications are subcutaneous (administered with a small needle under the skin). As part of the orientation process will make sure you feel comfortable with administration of the injections.

- FSH *(Gonal-F®, Follistim®,Bravelle®)* - These medications contain only FSH and are administered on a daily basis by injection.
- LH *(Luveris®)* – This medication contains only LH and is administered by injection. It is used in combination with FSH containing medications.
- Human Menopausal Gonadotropins *(Menopurl®,Repronex®)*- These medications contain equal amounts of FSH and LH, and are administered on a daily basis by injection.

Human Chorionic Gonadotropin (HCG)

Human chorionic gonadotropin or hCG mimics the natural LH surge that leads to ovulation. HCG is available as a urinary extract under the brand names Novarel™, Pregnyl® or Profasi® or in recombinant form, Ovidrel®.

Medications that prevent a premature ovulation

GnRH Agonists

These medications are used to help get better control of the cycle and prevent premature ovulation. The most commonly prescribed medication is Lupron® (given by injection).

GnRH Antagonists

Cetrotide® (Cetrorelix) is available both as a 3-mg single subcutaneous injection that lasts for 4 days and 0.25 mg meant for daily subcutaneous injection.

Ganirelix is available at a dose of 0.25 mg (prefilled syringe) for daily subcutaneous administration.

Other Medications

Some women may benefit from other medications given during the stimulation phase of treatment while others may require supplementary medications after ovulation. The following list covers the most common adjunct medications prescribed during ovulation induction therapy.

Insulin Sensitizers

Insulin sensitizers are agents commonly used in women who have polycystic ovarian disease. The most common insulin sensitizers available today include Glucophage® (Metformin), Avandia® (Rosiglitazone) and Actos® (Pioglitazone). Of these three, Glucophage has the longest track record of success and is the most highly prescribed.

Progesterone

Progesterone may be offered to some patients following ovulation. Progesterone can be administered vaginally (Crinone®, Prometrium®, pharmacy compounded suppositories) or by intramuscular injection. Store at room temperature.

Storage of Medications

Gonadotropins: Luveris®, Gonal-F®, Bravelle®, Menopur® and Repronex® Lyophilized powder may be stored refrigerated or at room temperature 36°-77° F. Protect from light. Use immediately after reconstitution. Discard unused material. Follistim AQ-Cartridges should be stored in your refrigerator until ready to use.

Lupron

Lupron® 2 week kit: Store in refrigerator- needs to be protected from light and heat.
Keep below 77°F. Protect from light.

Cetrotide/Ganirelix

Protect from light. Store Cetrotide 0.25 mg vials in the refrigerator (keep from freezing) and store the 3 mg vials at room temperature. Do not store in the bathroom, near the kitchen sink, or in other damp places. Store ganirelix® at room temperature.

ADMINISTRATION OF INJECTIONS

You will speak with our patient liaison to learn more about the treatment and discuss how to administer the injections. Please contact patient educational services at **781-434-6524** several weeks before you plan to start treatment. To learn more about injections we encourage you to visit a number of websites that are informative:

- ***www.villagepharmacy.com*** and click on "Video injection lessons" then enter the user id code **"Village1"** and password **"fertility"** once you have entered please select the medication video that has been prescribed for you.

- ***www.freedommedteach.com*** is another injection website that is informative. You will need your prescription number in order to view the medication injection videos this can be obtained on your prescription.

Administration of subcutaneous injection

1. Choose an injection site
   - back of upper arm
   - fold of abdomen 2 inches parallel to or below the belly button
   - Side of upper thigh
2. Swab the area with alcohol. Allow the area to dry. Avoid any area that has a bruise, mole or obvious blood vessels. Some patients have reported less stinging, burning, and redness when they use the abdomen.

3. When the site is dry, pinch a fold of skin. If using the abdominal site, use the area two (2) inches to the right or left of the umbilicus. If using the thigh, use the upper outer portion of your thigh. Do not use the inner thigh area.

4. Use your other hand to insert the needle straight into the injection site.

5. Release the pinch and slowly depress the plunger all the way and remove the needle.

6. Use a clean gauze pad to stop any bleeding that may occur.

CYCLE MONITORING

In order to monitor the response of the ovaries to gonadotropins, ultrasound examination of the ovaries and/or measurement of blood hormone levels are performed. The number of ultrasound examinations and blood tests varies from cycle to cycle. The average number of tests per cycle is 3-4.

The ultrasound examination is done using the vaginal ultrasound technique. A vaginal probe is placed into the vagina and visualization of the ovaries is obtained. Follicles are fluid-filled cysts in the ovaries in which the egg develops. The size of the follicle is related to the maturity of the egg. The number and size of the follicles are recorded by ultrasound. The objective is to obtain a number of follicles of sufficient diameter to result in a mature egg. A mature follicle is between 15-22 mm in diameter. Since the ultrasound is performed transvaginally, there is no need for a full bladder.

In addition to the ultrasound examination, blood tests are sometimes performed to measure blood hormone levels, including estradiol (estrogen). The developing follicles produce estradiol in response to gonadotropins. Therefore, estradiol determinations allow the physician to obtain further information about ovarian response. You will be given an appointment for your blood test and ultrasound examination. The ultrasounds and blood tests are scheduled early in the morning so the results are available early in the afternoon.

Monitoring with a Urine Ovulation Predictor Kit

When a non-medicated approach or clomiphene citrate is prescribed, an ovulation predictor kit may be used to determine the timing of ovulation for intrauterine inseminations. You will be given instructions on the day to start testing your urine. Specific instructions are as follows:

1. The urine testing should be done in the morning after discarding your first morning urine.

2. Once the test has turned positive, the IUI will be scheduled the following day as follows:

    - If the test is positive on **Monday-Friday**, you should contact your nurse to schedule an IUI for the following day. Confirm the specimen drop off, collection time and location with the nurse. Also confirm the location of the center where you will have your IUI performed.

    - If the test is positive on **Saturday, Sunday or a holiday**, you should call the Boston IVF, Waltham Laboratory at (781) 434-6431.

- Leave a message on the answering machine including your name, your doctor's name, and your date of birth and that you will need an insemination the following morning. Ask to be called back when the lab staff arrive or call the lab again after 7:30 a.m.

Timing of Intercourse or Insemination

Gonadotropin therapy allows for more precise timing of intercourse or insemination treatments. Insemination treatments (donor or partner) are usually performed approximately the day after detection of an LH surge when using an ovulation predictor kit or approximately 12 and 40 hours after the hCG injection. If conception will be attempted through relations, then intercourse should occur 1-3 times during the two consecutive days after hCG administration or the day of and/or day after the color change in an ovulation predictor kit. In these cases it is not necessary to skip days in between relations. However, please avoid over the counter vaginal lubricants. Use natural glycerin oil if vaginal lubrication is needed.

INTRAUTERINE INSEMINATION (IUI) PROCEDURE

Intrauterine insemination (IUI) is a technique for introducing sperm into the uterine cavity. Normally, during intercourse, sperm are deposited in the vagina near the cervix (the opening to the uterine cavity). With IUI, the sperm are introduced through the cervix directly into the uterine cavity. IUI may be used in a natural cycle, or along with medications such as gonadotropins or clomiphene citrate. The IUI is timed around the time of ovulation. This procedure is simple, relatively painless and takes only minutes to do. A trained medical assistant or nurse performs the IUI in the office.

TECHNIQUE OF IUI

You should plan on being at the office for approximately one hour (this includes waiting time) as sperm preparation may take 45 minutes or more. Appointments are scheduled in advance but we are flexible with scheduling as your day of ovulation may be different than predicted. In general, an IUI is performed once or twice in a treatment cycle.

Your partner can produce the sample on site or it can be produced at home as long as it can be delivered to the lab within an hour after it is produced. During transport the sample must be kept at body temperature. **It is our policy that the male partner drops off the semen sample at the andrology lab. At the time of delivery identity will be verified by a driver's license.**

Upon arrival, the specimen will be analyzed and then prepared. This will take approximately 45 minutes. Your partner does not need to accompany you to this appointment, although of course he is welcome.

A speculum is inserted and a small plastic catheter (tube) is introduced through your cervix into your uterus. The sperm is then injected into the uterine cavity. Occasionally, a gently placed clamp is needed to steady your cervix and allow for proper placement of the specimen. This process takes only minutes and you may leave immediately after the procedure.

Most women feel little or no sensation during IUI. At most, patients report a mild menstrual-like cramp. However, occasionally more severe cramping is felt. In rare cases, a woman may feel lightheaded, dizzy and faint. These symptoms may indicate a "prostaglandin reaction". This is a response to a substance in the seminal fluid, which in rare cases can produce such symptoms. This problem generally reverses itself rapidly and occurs only in approximately 1% of patients. Occasionally an antiprostaglandin medication such as ibuprofen (Advil, Motrin) can reverse these symptoms.

One complication following the IUI is the development of an infection. If you develop any abdominal pain, fever, chills, unusual or foul-smelling discharge, please call the office.

Where can I go to have the IUI performed?

The IUI can be performed at several of our centers (*Please note that if you using donor sperm or a frozen sperm sample all inseminations must be done at our Waltham location*):

Monday-Friday: Brookline, South Shore and Waltham centers are all available.
Weekends and Holidays: Waltham center only.

DONOR INSEMINATION

- Prior to starting your cycle, confirm that the sperm you intend to use has been received by our laboratory or is in storage in our laboratory.
- Call with the onset of your menstrual period and speak to your treatment team for instructions.
- If you are using an ovulation predictor kit to determine the timing of ovulation for intrauterine inseminations. You will be given instructions on the day to start testing your urine. Specific instructions are as follows:
    - The urine testing should be done in the morning after discarding your first morning urine.
    - Once the test has turned positive, the IUI will be scheduled the following day as follows:
        - If the test is positive on **Monday-Friday**, you should contact your nurse to schedule an IUI for the following day.
        - If the test is positive on **Saturday, Sunday or a holiday**, you should call the Boston IVF, Waltham Laboratory at (781) 434-6431.

          Leave a message on the answering machine including your name, your doctor's name, your date of birth and that you will need an insemination with a donor sperm sample the following morning. Ask to be called back when the lab staff arrives or call the lab again after 7:30 a.m.

3. All donor insemination procedures are performed at the Waltham center.
4. Your message to the laboratory should specify donor insemination.
5. If you plan to bring your frozen donor specimens with you, inform the laboratory as above and deliver the specimen to the laboratory between 7:00 - 8:30 a.m.

COMPLICATIONS OF TREATMENT

Two important side effects of using the fertility medications as described below are ovarian hyperstimulation and multiple pregnancy. Other side effects of the treatment are described in the consent form.

Ovarian Hyperstimulation

Gonadotropins and rarely clomiphene citrate can occasionally cause hyperstimulation of the ovaries. This means that the ovaries are especially sensitive to the medication and enlarge with temporary cysts. To decrease the risk, your physician prescribes the lowest possible dose of medication. When taking gonadotropins, your response is monitored with ultrasound and estradiol blood tests.

Even with careful monitoring, occasionally some women do develop hyperstimulation. Hyperstimulation usually occurs 5 or more days after ovulation or after the hCG injection. Usually, this problem will reverse itself without treatment within in 2-3 weeks. Please check for the following signs and symptoms, which may indicate hyperstimulation. If you develop any of the following symptoms, please call your physician as soon as possible.

> ***Weight Gain:*** A weight gain of two pounds or more for two days in a row may be a warning sign. Please weigh yourself daily and report any sudden or rapid weight gain.
>
> ***Abdominal Pain:*** While mild bloating and cramping may be normal, watch for excessive bloating, or unusual tenderness or pain in your abdomen. Sometimes abdominal pain is accompanied by nausea, vomiting and/or diarrhea.
>
> ***Urine Output:*** Please let us know right away if you notice any obvious change in urine output, either an increase or decrease. At the same time, check for signs of bladder infection (burning, painful or frequent urination).
>
> ***Shortness of Breath:*** If you have any difficulty breathing, either at rest or during activity, please report this at once.

If you notice any of the above symptoms, call your physician as soon as possible. A simple physical exam is sometimes all that is needed to check for hyperstimulation. In some cases, a pelvic ultrasound and/or blood tests are also necessary.

If hyperstimulation is mild to moderate, you will be asked to return to the office within the week for another exam and possibly an ultrasound. You will be asked to continue to check your weight every morning to be sure you are drinking and urinating properly. If hyperstimulation is severe, your doctor may advise you to have an outpatient procedure to drain some of the excess fluid that can collect inside the abdominal cavity that causes bloating and pain. This procedure may allow the hyperstimulation to resolve quicker and usually improves your symptoms. In addition to the above advice, you will be placed on

bed rest. In rare cases, hospitalization is necessary to more accurately monitor weight changes and ovarian status. There is a remote chance of severe illness, such as bleeding from the ovary, blood clots, kidney failure, etc. With current experience with these medications such effects are extremely remote. In the presence of hyperstimulation, it is important to avoid strenuous activities, either work or sports related. In addition, heavy housework that involves pushing or lifting (e.g., vacuuming) should he avoided. Intercourse is not advised in cases of moderate to severe ovarian hyperstimulation. Pregnancy can occur (possibly more readily) in the presence of hyperstimulation. Therefore, it is important to have a blood test for pregnancy if ordered by your physician.

MULTI-FETAL PREGNANCY

Multi-fetal Pregnancy

The advent of modern fertility treatments has lead to a substantial increase in the frequency of twins, triplets, quadruplets, quintuplets and even higher order multiples as shown by the birth of septuplets in Iowa in 1997. Multi-fetal pregnancy refers to a pregnancy in which two or more fetuses are present in the womb.

In the general population, multi-fetal pregnancies occur in approximately 1 to 2 percent of all pregnancies. However, with the use of fertility drugs such as clomiphene citrate or gonadotropins (FSH) and high-tech procedures such as in vitro fertilization (IVF), multiple gestations are much more common. The vast majority of these pregnancies are twins, but triplets, quadruplets and higher numbers can occur. Triplets and higher order multi-fetal pregnancies occur in 3% to 4% of couples undergoing IVF, and in 7% to 8% of patients undergoing ovulation induction with injectable FSH preparations.

Fetal and Maternal Risks

Fetal risks of multiple gestations include an increased chance of miscarriage, birth defects, premature birth and the mental and/or physical problems that can result from a premature delivery. The average length of pregnancy is 40 weeks for a single gestation; 36 weeks for twins; 33 weeks for triplets; and 29 weeks for quadruplets.

Triplet pregnancies have a perinatal mortality rate up to 12 times higher than that of singletons and 10% of triplets die at or about the time of birth. Quadruplet pregnancies are even more risky - women with quadruplet and higher order gestations deliver prematurely and of those that reach 24 weeks' gestation, approximately 25% of babies will die at or about the time of birth. For those babies that do survive they are far more likely to be handicapped by cerebral palsy, kidney failure, blindness and mental retardation. Maternal risks due to multiple gestations include premature labor, premature delivery, pregnancy-induced high blood pressure or pre-eclampsia (toxemia), diabetes and vaginal or uterine hemorrhage.

Reasons for Increased Risks

The uterus can normally increase its blood supply to nourish about 10 pounds worth of baby or babies. The uterus usually accommodates twins well but twin pregnancy is still associated with greater risk to the mother and babies than is a singleton pregnancy.

However, more than two babies can be problematic. As stated above, studies and surveys indicate that, on average, triplets are born seven weeks early, weighing 3.5 to 4 pounds. Quadruplets tend to be born 11 weeks early, weighing 2.8 to 3.5 pounds. Their prematurity is almost certain even though most of their mothers rest in bed for months, wear home monitors to count contractions and take drugs to ward off early labor.

Multi-fetal Pregnancy Reduction

Multi-fetal pregnancy reduction (MFPR) is a technique that reduces the number of fetuses in an effort to increase the likelihood that the pregnancy will continue safely. Consequently, the risks to the mother and remaining fetuses are reduced. The first multi-fetal pregnancy reductions were performed between 1986 and 1988, and since then, thousands of patients have had the procedure performed successfully.

The procedure is more likely to be performed when there are three or more fetuses present. The number of fetuses is usually reduced to two although in some circumstances they may be reduced to one. Because twins generally do better than higher order multiples, reduction in these cases is more individually determined and may be considered.

Timing and Technique for MFPR

Multi-fetal pregnancy reduction is usually performed between nine and twelve weeks gestation but it has been performed as late as 24 weeks gestation. The procedure is most successful when performed early in pregnancy on an outpatient basis. Anesthesia is usually administered and includes a mild sedative along with local skin infiltration.

According to some studies, the optimal number of fetuses following the MFPR procedure appears to be twins, since the outcome with twin pregnancies is generally good, and appears to be similar to the outcome for pregnancies reduced to singletons.

The risk of an induced miscarriage related to MFPR is 8% to 9%. Although this is a significant risk and must be considered before undertaking the procedure, the risk is not higher than the 10% fetal loss rate found in twin gestations following assisted reproductive technology. Maternal infection rarely occurs and injury to a surviving (non-reduced) fetus is considered to be highly unlikely.

Counseling

The best time to consider MFPR is prior to starting treatment. Dealing with the decision of whether or not to undergo multi-fetal pregnancy reduction can be an emotionally traumatic experience. Couples who have invested a great deal of time, energy and money in pursuing pregnancy are often unprepared to make this decision. It is usually helpful for couples considering multi-fetal reduction to undergo professional counseling prior to undergoing the procedure.

Both partners need to be comfortable with their decision and may need emotional support prior to and immediately following the procedure. The decision to proceed with MFPR is made with the intent to give a better chance of survival for the remaining babies from high order multiple gestations and reduce the likelihood of significant mortality and morbidity associated with these pregnancies.

Conclusion
MFPR has become an accepted procedure that can be performed safely with technical success. In select patients with higher order gestations, it provides an intervention that increases the chance of achieving the desired outcome (taking home a healthy newborn) while minimizing the associated risks of multi-fetal pregnancy.

Telephone Contact During Treatment

Patients undergoing daily injections of gonadotropins will receive a call with instructions as to the dose of medication required that evening. Please make arrangements to be available for that phone call. The dose of gonadotropins may be reduced, increased or maintained at the same level. Please be sure to have at least a two day supply of gonadotropins available should you be told to take that dose or a slightly increased dose. This avoids you having to rush to the pharmacy late in the afternoon for your evening dose of gonadotropins.

Follow-up Examination
One week after the hCG administration, you may be instructed to visit the physician for an "ovary check." This is to ensure that the ovaries have not over-responded. This visit is not always necessary.

Cycle Cancellation or Conversion to IVF
If the ovaries over-respond and there are too many follicles or the serum estradiol is too high, then the cycle may be cancelled. The reason for cancellation is to avoid ovarian hyperstimulation and the risk of a multiple pregnancy. In the unlikely event that your cycle is cancelled, you would be expected to wait at least one month before starting another gonadotropin cycle to allow the ovaries to return to their normal size.

An alternative to cycle cancellation in some cases is conversion to IVF. In the case of converted cycles, the eggs are retrieved prior to their release from the ovaries. This reduces the risk of multiple pregnancy since we can limit the number of embryos that are transferred back to your uterus. It also reduces the risk of developing ovarian stimulation syndrome. If you are a candidate for cycle conversion, your nurse will discuss it with you. Please be aware that some insurance companies will not cover the costs associated with a cycle conversion. In these cases you will be responsible for the cost of conversion to IVF. It is important to speak with a financial counselor about cycle conversion.

Conclusion of the Gonadotropin Cycle
If you get a period at the end of your cycle, you may be able to start another cycle or you may be asked to take one month off. That decision is based upon your response and we incorporate the information that we gained from the completed cycle in planning subsequent attempts. As pregnancy can occur in the presence of bleeding we encourage you to schedule a pregnancy test by calling your nurse. The pregnancy test should be performed no earlier than 14 days after your hCG or Ovidrel injection but can be performed somewhat later.

TIMELINES

Timeline--GONADOTROPIN with either IUI or RELATIONS

WHEN YOUR PERIOD STARTS

1. Call your nurse with the first heavy day of your menstrual period—this is considered cycle day 1. **If you menstrual period starts after 4pm---call the next day to speak to a nurse.**

2. **Do not page the doctor on call after hours to report the onset of menstruation.**

3. Your nurse will review with you the timing and dosages of the medications to be administered. She will also schedule blood tests and ultrasound exams that your doctor has ordered.

4. Administer the injections at the same time between 5-10 p.m.

5. The first ultrasound and/or blood drawing usually occur after taking 4 to 6 days of medication. Make sure to eat breakfast before having blood drawn.

6. A nurse will call you with your test results. It is critical that you leave an appropriate contact phone number if you will not be available at the home or office phone numbers that you have previously provided.

7. **If you do not hear from your nurse by 4 pm, please call in to check your instructions.**

8. On the day of the hCG injection to trigger the ovulation you should stop all other fertility medications.

9. IUI procedures will be performed approximately 12 and 40 hours after administration of the hCG.

10. A fresh semen sample will be needed on the morning of each IUI procedure. **The male partner must deliver the semen specimen to the laboratory.**

11. The IUI procedures are usually performed by nurses seven days a week including weekends and holidays.

    - On weekdays—the IUI can be performed at the Boston, Quincy and Waltham centers. .
    - On weekends and holidays—the IUI will be performed at the Waltham center only.

12. If your doctor recommends intercourse (instead of IUI) plan to have relations 1-2 times in the 6 to 40 hours after hCG administration.

13. If your doctor has prescribed progesterone it should be started three (3) days after the hCG injection. Do not stop progesterone therapy, even if bleeding occurs, until you have spoken with your nurse.

14. A pregnancy test is routinely recommended 16 days after hCG is administered even if you experience vaginal bleeding.

TIME LINE - CLOMID with either IUI or RELATIONS

WHEN YOUR PERIOD STARTS

1. Call your nurse with the first heavy day of your menstrual period—this is considered cycle day 1. **If you menstrual period starts after 4pm---call the next day to speak to a nurse.**

2. **Do not page the doctor on call after hours to report the onset of menstruation.**

3. Your nurse will instruct you when to start the Clomid and when to start the testing with the ovulation predictor kit or come in for monitoring with ultrasound exams and blood work..

    a. If you use the ovulation predictor kit please follow the instruction on page 8.

    b. If you are being monitored with ultrasound exams and blood work a nurse will call you with your test results and further instructions in the afternoon between 2 and 4:00 p.m. It is critical that you leave an appropriate contact phone number if you will not be available at the home or office phone numbers that you have previously provided.

4. ***If you do not hear from your nurse by 4 pm, please call in to check your instructions.***

5. On the day of the hCG injection to trigger the ovulation you should stop all other fertility medications.

6. IUI procedures will be performed approximately 12 and 40 hours after administration of the hCG or on the day after a positive test by the ovulation predictor.

7. A fresh semen sample will be needed on the morning of each IUI procedure. **The male partner must deliver the semen specimen to the laboratory.**

8. If your doctor recommends intercourse (instead of IUI) plan to have relations 1-2 times in the 6 to 40 hours after hCG administration.

9. If your doctor has prescribed progesterone it should be started three (3) days after the hCG injection. Do not stop progesterone therapy, even if bleeding occurs, until you have spoken with your nurse.

10. A pregnancy test is routinely recommended 14 days after the IUI.

SEMEN COLLECTION INSTRUCTIONS

1. Abstain from ejaculation during the 24 hours prior to semen collection.

2. Semen samples are produced by masturbation. Sterile specimen containers should be obtained from your local pharmacy or Boston IVF. Samples collected in non-sterile containers cannot be used due to the risk of bacterial contamination.

3. Please wash your hands before collection, making sure to remove all soap afterwards. Be certain not to touch your mouth, nose or rectal area after you have washed your hands since this could contaminate the semen with bacteria.

4. Do not use saliva, oils or lotions as a lubricant. If a lubricant is needed, please only use plain glycerin, this can be purchased at your local pharmacy.

5. If you live within a 60 minute drive of Boston IVF, you may produce your specimen at home. Please be sure not to expose the sample to excessive heat or cold by keeping it close to your body (in a shirt pocket or inside your shirt) to maintain an ideal temperature.

6. We request you print the following information on the specimen container and the lid.
    i. • your first and last name
    ii. • your partner's first and last name
    iii. • your partner's date of birth (month, day and year)

7. Please do not leave the specimen without confirming the above information with a lab employee.

8. The male partner must deliver the semen sample to the laboratory at least 1 hour and 15 minutes before the scheduled IUI. The sample can be dropped off as early as 7AM. **Identification will be verified by presentation of a driver's license.**

DIRECTIONS

Please visit our website for directions to the Boston IVF centers

THE DOCTOR ON CALL

For your safety, there is a Boston IVF doctor on call 24 hours a day for medical emergencies only. Please address all routine questions including test results and cycle starts with the office staff during business hours (9 am to 4 pm) Mon – Fri. Nurses are also available for questions 9 am to 3 pm on weekends and holidays.

