GENERAL FERTILITY - PATIENT INFORMATION BOOKLET

Version G

New Leaders In Fertility & Endocrinology

"NewLIFE"

FELLOWSHIP-TRAINED & BOARD CERTIFIED REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY SPECIALISTS

New Leaders In Fertility & Endocrinology, LLC
"New LIFE"

Dear NewLIFE Patient:

On behalf of our entire staff we would like to welcome you to our practice.

The following information is provided for your review and is a general guide for common testing and progress toward fertility treatment. We ask that you read carefully all sections, making notes or writing questions in the margins. Bring this booklet to your subsequent visits as a reminder. The booklet will answer the most common questions patients have about fertility. Sometimes you may feel a bit overwhelmed by the paperwork, but it is an important first step.

Studies in the United States have shown that of the 2.4+ million infertile people each year (that is about 10% of all reproductive age couples), only half will seek a physician's evaluation. More importantly, those same studies suggest that for those who seek and receive care, the majority will achieve a successful pregnancy. With this first step you have joined that "take charge" and confident majority!

We truly appreciate the effort required to make progress and hope you will continue on this road to success. Be assured that our entire staff is able and available to help you along your journey.

Warmly,

The NewLIFE Staff

New Leaders In Fertility & Endocrinology
MISSION STATEMENT

Our goal is to provide infertile patients with progress toward a successful pregnancy, as promptly, gently and as cost effectively as possible.

GENERAL OFFICE ISSUES (PLEASE READ CAREFULLY)

The following describes many important topics and concerns for patients. Please read each carefully and adhere to the recommendations provided.

1) Office Visits: That you are reading this booklet probably means that your initial consultation has been arranged. During the next few weeks additional information will be gathered about you and when completed, treatment planning will be scheduled. At this time, test results and various treatment options or additional testing will be discussed. Decisions will often be at this time to begin selected treatment(s) or to complete additional test such as laparoscopic surgery. Many factors will affect this decision including; what is the suspected cause(s) of infertility, available insurance coverage, effectiveness of specific treatments and the couples own emotional strength and available time commitment. This is a good time to bring up any questions that arise after reading this booklet, as you will be asked to acknowledge your understanding of this material.

2) Patient Responsibilities: Contrary to popular belief, a physician's skill alone, rarely cures illness but also requires the patient's own healing processes. Nowhere is this more evident than in the treatment of infertility, where a TEAM EFFORT is needed. Physicians and nurses will provide the necessary information, training, counseling and guidance but this is ineffective without patient's commitment to educate themselves and become compliant and knowledgeable about fertility treatment. Thus, various educational videotapes, patient information booklets and American Society of Reproductive Medicine pamphlets will be provided, as needed. It remains a patient's responsibility to read and understand these materials, asking questions when needed. Because of the time limitations and volume of patients involved, these written materials should be your first reference and questions that remain should be brought to subsequent visits. It is difficult, if not dangerous, to offer complex treatment or information to patients by telephone alone, or by fax, electronic or recorded messages.

3) Communication with the office: During treatment it is vitally important that the office have an effective way to provide instructions to you. Active telephone numbers and one back up number with a private answering device (home, work, mobile phone, voice-mail) are required. Provide written request if certain telephone numbers should not be used. If you have pressing questions not answered in the patient information materials, please call and leave a DETAILED message with the office. Messages will be assessed and answered in an order based on the information provided. Lab results are rarely given by telephone and will not be interpreted by non-medical office personnel. Giving a single test result out of context to other findings can be misleading. We attempt to present and discuss all related findings together at a single visit. Please notify the office during business hours of the onset of menstrual periods, ovulation surges and other important developments. Please keep numbers handy for our offices in:

Pensacola, Panama City, Tallahassee, Florida, and Mobile and Dothan Alabama, and Biloxi Mississippi

For urgent matters after office hours, scheduling or instructions call the **Doctor's Directory at 850-444-5507** and a text message will be sent to the on-call medical personnel at your location. **NOTE:** non-urgent calls made after-hours may generate a professional fee. Thus, wait to call during regular office hours. For true emergencies, call 911. (Do not call an office, as this delays getting help)

4) Insurance: Despite diligent efforts to assess your insurance coverage, neither you as a consumer, nor we as a medical office can be assured of reimbursement for infertility services. This is an unfortunate consequence of the current philosophy of the insurance industry and its attitude towards fertility care. There may be expenses not covered by insurance (see insurance section).

5) Stress and Anxiety: The entire NewLIFE Team makes efforts to reduce the frustrations common to the situation. Regardless of one's emotional strength, the "fertility journey" may become a significant stressor for couples. It is common for patients to need extra support during this time. Access to professional counselors is encouraged, frequently recommended and occasionally required for some treatments. Referral to this helpful resource is usually received with a sigh of welcome relief, as many couples are reluctant to talk about it. Stress management may have more than mental benefits, as some published reports suggest pregnancy may be more likely with counseling! There are many counselors who are experienced with fertility and offer assistance to patients.

6) Primary Care Physicians and Referring Ob/Gyns: When referred for infertility sub-specialty care, we act as a consultant only. Thus, you should keep routine check ups and visits with your Ob/Gyn or primary care physician, particularly for common gynecologic conditions: vaginal infections, PAP smears, mammograms, etc. You will be referred back to your Ob/Gyn during the first trimester when conception has been confirmed and after a reassuring ultrasound.

INFERTILITY AND YOUR INSURANCE COMPANY

Insurance benefits are often difficult to define and interpret. Our office staff will attempt to contact your insurance company but if you are inclined, here are some important questions to ask your insurance representative:

1. Is there a specific person that handles questions regarding infertility coverage? Request your insurance company policies regarding infertility, in writing. This may be found in the "exclusions" paragraphs located in your Benefits Booklet
2. Is there a limitation on pre-existing conditions?
3. What percent of fertility medicines, office visits and procedure expenses are covered?
4. Is there a different co-payment for infertility services? For medication?
5. What is the annual deductible per person? Per family?
6. Is there a maximum out-of-pocket expense you can incur in a single year?
7. Is pre-authorization required for any particular service or procedures?
8. What **specific** procedures should be followed when filing a claim?
9. Is there a particular pharmacy you must use for medication? Where is it located? Are injectable drugs obtained differently? Is there a prescription drug limit?
10. Is there a limited length of time you can be treated for infertility?
11. Are counseling services covered? What is the coverage and guidelines to be followed?
12. Is a referral required to see a fertility specialist?
13. Is there a particular laboratory to be used?
14. Are the following Infertility Diagnostics covered?:
    Hormone tests, Genetic disease screening, Hysterosalpingogram (HSG), Semen analysis, Ultrasound, etc.
15. Are the following Infertility Therapies covered: Medications (i.e., Clomiphene, Gonal-F, Follistim), Ultrasounds, Blood work and Lab Tests, Intrauterine insemination (IUI), In Vitro Fertilization

IMPORTANT NOTICE
Despite answers to these questions by telephone, reimbursement from your insurance company is NOT guaranteed. There may be certain services that will be deemed as "unnecessary" or denied for coverage by your insurance company. As insurance companies cannot by law practice medicine, decisions for such services remain with you and your physician. However, as these services are considered effective and necessary for successful pregnancy, patients will be asked to cover their expense.

GENERAL INFORMATION ABOUT FERTILITY

What is infertility?

A "normal" couple has a 15-20% chance of becoming pregnant during any one menstrual cycle. Eighty to ninety percent of these couples should become pregnant during one full year. Infertility is common, with one out of every six couples having trouble conceiving and/or carrying a pregnancy to delivery. **Infertility is defined as the failure to become pregnant after one year of unprotected, well-timed sexual intercourse.** This and failure to conceive in 6 months for a woman less than age 30 or 2 consecutive miscarriages are considered reasons to seek evaluation. Infertility more than 2.5 million people each year in the United States which means you are NOT alone.

What causes infertility?

Natural pregnancy follow a series of steps, each being required for normal conception. Ovulation is complex and dependent on the action of hormones released by the ovary, the pituitary gland and a part of the brain called the hypothalamus. Ovulation usually occurs about fourteen days before the next menstrual period. When released from the ovary, an egg is swept into a fallopian tube where fertilization may occur, if healthy sperm are available. Just a few of the total number of sperm released into the vagina actually survive to arrive in the fallopian tube. Five to seven days after ovulation, a fertilized egg (embryo) implants in the lining of the uterus where nourishment can maintain its continued development.

Studies have found that about 60% of infertility is caused by female factors, 40% by male factors, and 20% by a combination. Defects in almost every step have been reported and any one defect may result in decreased fertility. Common causes of infertility include hormone dysfunction, blocked or damaged fallopian tubes, pelvic adhesions, endometriosis, and abnormal or decreased numbers of sperm and poor cervical mucus. Thus, a very thorough approach must be taken to accurately diagnose the cause(s) of infertility.

How is infertility evaluated?

To determine causes of infertility, we use your medical history, physical findings and results of diagnostic testing. This is called an **infertility work-up.** Specific diagnostic tests are selected based on this information and on previous testing and/or treatment. These might include blood testing of hormones and others factors, vaginal ultrasounds, hysterosalpingogram (HSG), diagnostic laparoscopy and/or hysteroscopy, endometrial sampling, semen analysis and other tests.

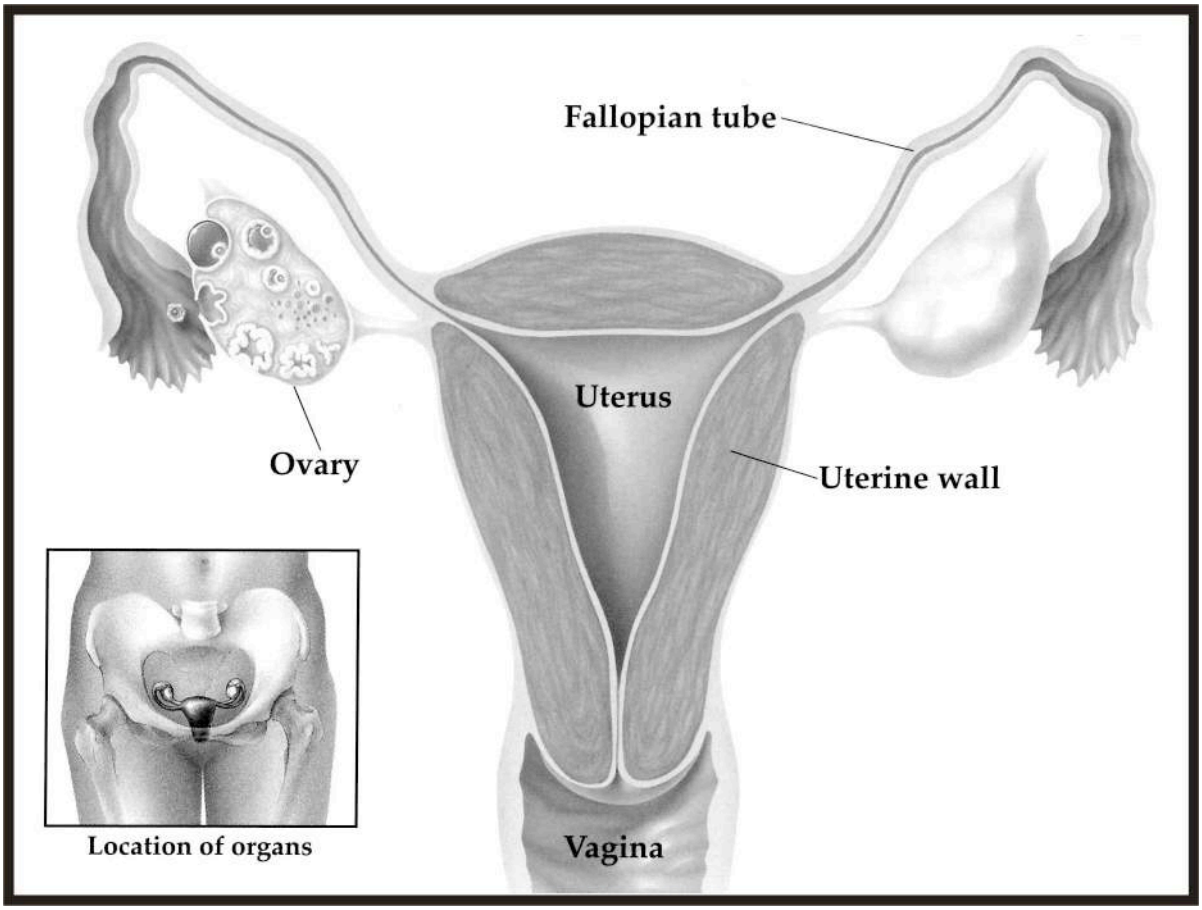
What is the next step?

After your infertility work-up, all results of your tests will be reviewed with you during a return office visit and various options for treatment will be offered. We do not usually discuss an individual test result until all of the others are available, as one may mislead interpretation without the others. When available your physician will meet to discuss everything found. This visit is called “Treatment Planning” or a “Treatment Plan”. Your input, feelings and understanding are very important in making a decision about treatment. We encourage you to visit as a couple whenever possible and to ask questions, keep notes and follow directions. It is vital that you keep us informed of your status: INFERTILITY TREATMENT IS PATIENT INITIATED.

NORMAL OVULATION & CONCEPTION

The Process

The ovaries are two small glands, each about one-and-one half to two inches long and three-fourths to one inch wide, located in a woman's pelvic cavity (Figure 1). They are attached to the uterus (womb), one on each side, near the fimbriated (finger-like) openings of the fallopian tubes. About once a month, a mature egg is released by one of the ovaries. The fimbriae of the fallopian tubes sweep over the ovary and pick up the egg after it has been released from the follicle (the fluid-filled ovarian cyst containing the egg). If the egg is fertilized, which usually occurs in the tube, the resulting embryo (fertilized egg) continues to mature and increase its number of cells as it travels to the uterus and implants in the endometrium (uterine lining). The embryo's full journey through the tube takes four to five days.



Hormone Production during the Menstrual Cycle

In addition to producing eggs, the ovaries also secrete hormones. Hormones are substances secreted from organs of the body, such as the pituitary gland, adrenal gland, or ovaries, which are carried by a bodily fluid such as blood to other organs or tissues where the substances exert a specific action. The cycle of ovarian hormone production has two main phases. During the first phase, known as the follicular phase, an egg matures inside the ovary. The egg is surrounded by a layer of hormone-producing cells and by fluid. The maturing egg, the surrounding cells, and the fluid are collectively known as a follicle. The follicle grows to a diameter of about an inch, forming a cyst-like sac on the surface of the ovary, before the fluid and the egg are released at ovulation.

In natural cycles, an ovary contains several developing follicles, but usually only one follicle reaches maturity each month and releases an egg. This follicle, known as the dominant follicle, secretes a generous amount of the female

hormone estradiol (estrogen) into the bloodstream during the first phase of the cycle. The estrogen circulates to the uterus where it stimulates the endometrial cells to reproduce rapidly and repeatedly, causing the uterine lining to thicken as ovulation approaches. The physician can usually see this thickening on an ultrasound exam.

The second phase of ovarian hormone production begins with ovulation. The dominant follicle ruptures, usually around day 14 in a 28-day cycle, and releases a mature egg onto the surface of the ovary near the fallopian tube. The empty follicle collapses and the remaining follicle cells develop a yellow color. Collectively these cells are known as the corpus luteum, literally a "yellow body." The corpus luteum secretes estrogen and large quantities of progesterone throughout the second half of the cycle, known as the luteal phase, which lasts approximately two weeks.

Traveling through the bloodstream to the uterus, the combination of progesterone and estrogen causes the uterine lining to further mature and produce nourishment for an embryo. About a week after ovulation, the endometrium is in prime condition for an embryo to implant. An experienced physician can tell approximately how many days have passed since ovualtion by examining a sample of the endometrium taken in a biopsy. If no embryo implants, the secretion of estrogen and progesterone declines about two weeks after ovulation and, as a result, the endometrium is shed. This shedding of the endometrium is called menstruation.

The first day of menstruation is known as "cycle day one." The length of the menstrual cycle is determined by counting the number of days from cycle day one until the start of the next menstrual period. Although variability in cycle length is usually due to variablity in the follicular phase, the luteal phase can also be variable in length. The luteal phase should last 11 to 16 days. If it is not sufficient in length because of inadequate progesterone production, fertility problems may result. Since ovulation usually precedes menstruation by two weeks, a woman with a 28-day menstrual cycle is most likely to ovulate on day 14. Similarly, a woman with a 32-day cycle is most likely ovulate on day 18.

FINDING A CAUSE OF INFERTILITY: DIAGNOSTIC TESTS

Following your first consultation, it is likely that you will be instructed to begin or complete your fertility evaluation. Testing may include some or all of the following tests to determine a cause or causes of your infertility.

❖ HYSTEROSALPINGOGRAM (HSG) - RADIOLOGIC

Hysterosalpingogram (HSG) commonly called the "dye test" is used to discover if there is blockage of the fallopian tubes or abnormalities of the uterus and cervix. A dye visible to X-ray (or salt water, if ultrasound is used) is injected through the cervix into the uterus and fallopian tubes. This may cause cramping and pre-medication is recommended. The total procedure takes approximately half an hour. HSG's are scheduled between day 7 - 11 of your menstrual cycle, after menstrual flow ceases and before ovulation. If your menstrual flow is prolonged, the procedure may be postponed to the next month. If you are on birth control pills, it may be scheduled more readily in same month.

Risks to Patients
In addition to discomfort and bleeding, HSG may rarely result in perforation of the uterus or infection. Infection occurs in less than 1% of patients but can require hospitalization and intravenous antibiotics. Unfortunately, there are no simple alternatives to obtain this vital information. Patients are thus asked to monitor themselves after the test for any symptoms suggesting complications such as infection, fever, pain, bleeding.

Patient Instructions

1. Contact the office during the FIRST 3 days of your menstrual period. If this occurs on a weekend or holiday, please call the next business day.

2. Call the office to re-schedule your HSG appointment if you have not stopped bleeding on the day it is scheduled. The test cannot always be performed while you are actively bleeding. Let the office know if you take oral contraceptive pills.

3. You may be given an antibiotic prescription to take the morning of your procedure.

4. Take Advil® or Anaprox® (Naprosyn) with food or liquids at least one (1) hour before the procedure to minimize uterine cramping. Antibiotics may also be ordered for the morning of and evening after the procedure.

5. After the test you may experience cramping and spotting. If you develop a fever or bleeding becomes as heavy as the heaviest flow during your menstrual period **call the office immediately.** After office hours, or on weekends or holidays, call the Doctors Directory.

Special Situations

*** This procedure **cannot** be performed by x-ray dye if you are allergic to iodine or shellfish.
*** Inform the doctor if you have mitral valve prolapse, a heart murmur, or any other condition requiring antibiotic treatment before a medical procedure. An antibiotic prescription may be ordered for you.

Hysterosalpingogram ("HSG" or the "dye test")

❖ HYSTEROSCOPIC HYSTEROGRAM

Hysteroscopic hysterogram, or "hs-HSG". This new technique allows for assessment of the fallopian tubes without radiation or dye, and is usually completed with great ease. It is similar to the diagnostic hysteroscopy (see below), and is a relatively easy, short procedure completed with saline (salt water) and small air bubbles. Images are projected on a digital display allowing the patients to see the findings. No special preparation is needed, but unlike the Diagnostic Hysteroscopy, the hs-HSG is scheduled closer to the time of ovulation. The addition of air bubbles allows confirmation of flow of fluid into the fallopian tubes. If flow cannot be confirmed, an ultrasound may follow to determine if fluid is collecting at the end of a tube, called "hydrosalpinx." Occasionally, a standard radiologic HSG may be necessary to follow or ordered instead of the hs-HSG.

Risks to Patients
In addition to minor discomfort and bleeding, hs-HSG may rarely result in perforation of the uterus or infection. Infection occurs in less than 0.1% of patients but can require treatment, hospitalization and intravenous antibiotics. Patients are thus asked to monitor themselves after the test for any symptoms suggesting complications such as infection, fever, pain, bleeding.

❖ ENDOMETRIAL SAMPLE

The endometrial biopsy or sample can be used to evaluate the quality of ovulation by assessing the progesterone-induced changes inside the uterus and/or to exclude microscopic infection or inflammation, excessive growth (hyperplasia) or cancer in some women. It is rarely needed with current hormonal testing. After a negative pregnancy test, it is performed in the office 10-12 days after a positive LH surge or hCG injection. The procedure requires just a few moments with a speculum examination and the passage of a thin catheter through the cervix to obtain a small piece of tissue from the inner lining of the uterus. You may experience some menstrual-like cramping and discomfort during and after the procedure. It is recommended that you take ibuprofen or naproxsyn

with a light meal at least 60 minutes prior to the biopsy. You may have some light spotting after the procedure. Notify the nurse if bleeding becomes heavier than a menstrual period.

Risks to Patients
In addition to discomfort and bleeding, endometrial biopsy may rarely result in perforation of the uterus. Patients are asked to monitor themselves after the test for any symptoms suggesting complications such as infection, fever, pain, bleeding.

Patient Instructions
1. Notify the office of a positive LH surge to schedule the biopsy.
2. Take ibuprofen or naproxsyn with food one hour before the procedure.
3. Please call the office with the date of next menstrual period (normal flow).
4. Call the office if you experience any severe cramping, fever and/or heavy bleeding after the procedure. After hours or on weekends call the Doctor's Directory.

❖ SEMEN ANALYSIS

The **semen analysis** is the most important single test in the evaluation of the male, reporting the number of sperm, the percent of moving sperm ("motility"), their structure and shape ("morphology"), and the volume of the semen sample. Semen analyses are performed on SPECIFIC DAYS in each office. **Therefore**, **appointment times must be made for Semen Analysis**.

Written "Patient Instructions" will be provided to you when the test is requested, but general considerations are:

1. A semen specimen should be obtained following a two to four day period of sexual abstinence.

2. Avoid soaps, detergents, creams or lubricants to aid specimen collection. These agents may interfere with sperm motility. Assistance from the female partner is encouraged and may even improve semen quality.

3. Collect the ENTIRE specimen in the sterile container. The volume should be a little more than one-half teaspoon. Please let the lab know if any spillage occurred during specimen collection. **This is very important!**

4. The semen is ROUTINELY collected at home and should be delivered to the office/lab within as soon as possible after ejaculation. Keep the specimen close to body or at room temperature during transportation. **Do not put it near a heater!** Time is not as important as temperature when transporting semen samples, therefore, drive carefully.

6. Always label the specimen cup with your NAME, DATE and TIME of collection and number of days since last ejaculation. According to laboratory policy, specimens received without this information may be refused and may not be processed.

7. Be prepared to provide photo identification at the time of collection or drop of the specimen.

❖ ULTRASOUND

This painless procedure allows your physician to take pictures of your ovaries and uterus using supersonic sound waves. A small probe is placed in the vagina and images are displayed on a video screen during the exam and may be recorded on film. This test may also determine the thickness of the lining of the uterus, development of eggs in the ovary and identify uterine fibroids or other uterine abnormalities. There are no known risks to the use of ultrasound and the vaginal approach has made holding a full bladder unnecessary.

It is likely that ultrasound will be used many times during the fertility evaluation and is a vital tool for successful fertility treatment

❖ OVULATION DETECTION

In most ovulating women, the length of each menstrual cycle will range from 25 to 32 days. Ovulation occurs approximately 13-15 days before the next menstrual period. Keeping track of the length of menstrual cycles helps to determine the approximate time of ovulation. Ovulation predictor kits, which are available at most drug stores, are

also helpful in determining the approximate time of ovulation. These kits detect Luteinizing Hormone ("the LH surge") that is found in urine 12 to 40 hours before ovulation. Each kit contains 5 or 6 tests that are to be used on consecutive days until a positive test occurs. You should begin testing on cycle day 12 if your usual cycle is 28 days long.

Other Guidelines:

1. Use urine from the first time you go after getting out of bed in the morning (it's the most concentrated).
2. Read package directions carefully to be sure of accurate interpretation of test results.
3. Notify office when there is a positive test. It should be negative the FIRST day that you test.
4. If you are not having insemination, have intercourse the night of a positive LH and the following night.
5. When purchasing ovulation detection kits, the one-step kits that give results in 5 minutes are recommended. Read directions and purchase one that is EASY to use.

Other Methods of Ovulation Detection

Basal Body Temperature Charting (BBT) - helpful only if cycles are consistently regular and chart is consistently biphasic (elevated temperature after the first half of the cycle)

Endometrial biopsy - confirms adequate ovulation effect within the endometrial lining of the uterus but is not practical for use on a monthly basis.

Serum Progesterone Level - a single sample is helpful if within normal range and drawn on the correct day of the cycle. Serial sampling is more helpful and is may diagnose subtle ovulation problems and involves 3 random progesterone levels 5-9 days after a LH surge.

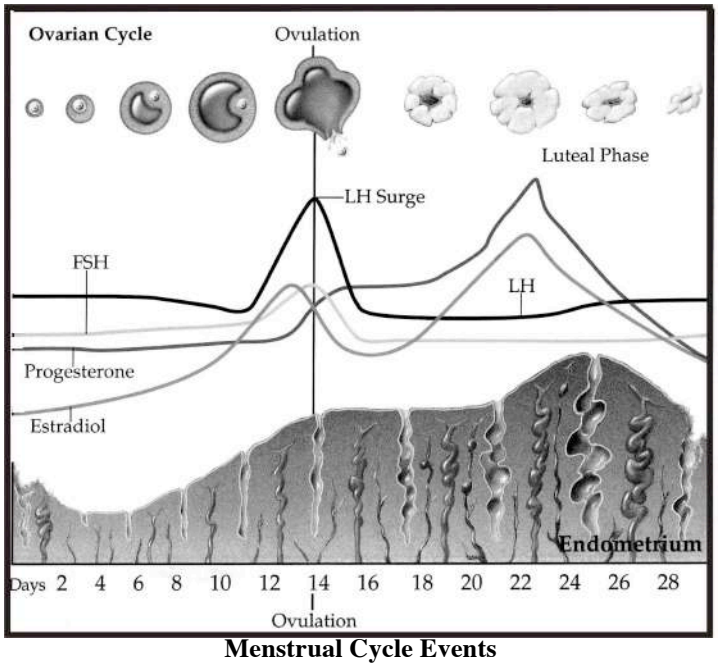
Positive Pregnancy Test - If this test is positive, you don't need ovulation kits. Ovulation has definitely occurred!

❖ OTHER PRE-PREGNANCY TESTS & SCREENING

Many other conditions and diseases can affect the outcome of pregnancy. It is routine to test for these PRIOR to use of fertility treatments to allow these conditions to be corrected or counseled. Examples include thyroid gland dysfunction, PCOS, tobacco exposure, vitamin D deficiency, lack of immunity to certain viruses, etc. Before treatment with IVF/ART, the FDA requires screening for infections and infectious diseases. Prospective parents are routinely offered screening to exclude being a carrier of a genetic disorder that has the potential to affect the health or life of a baby.

❖ DIAGNOSTIC CYCLE MONITORING

This test is performed to evaluate the components of your entire menstrual cycle and quality of ovulation. An instruction sheet will be given to you when this test is ordered and a calendar on the next page is helpful to schedule tests. The following illustration shows the normal rise and fall of hormones during a menstrual cycle.



Menstrual Cycle Events

❖ CYCLE MONITORING: BASIC INFORMATION

Cycle monitoring involves tracking the growth of ovarian follicles through blood hormone testing and ultrasound studies. It is necessary to follow the ovary's response to fertility pills and injectable medications. Monitoring allows adjustments in medication dosage and may help to avoid hyperstimulation or multiple pregnancies.

Monitoring usually begins within the FIRST few days after starting your menstrual flow and typically begins with a "baseline" vaginal ultrasound and blood tests. Monitoring during the rest of your cycle will depend on your individual mode of treatment and your response to treatment. clomiphene (Clomid®) cycles in general require less monitoring than cycles with fertility injections.

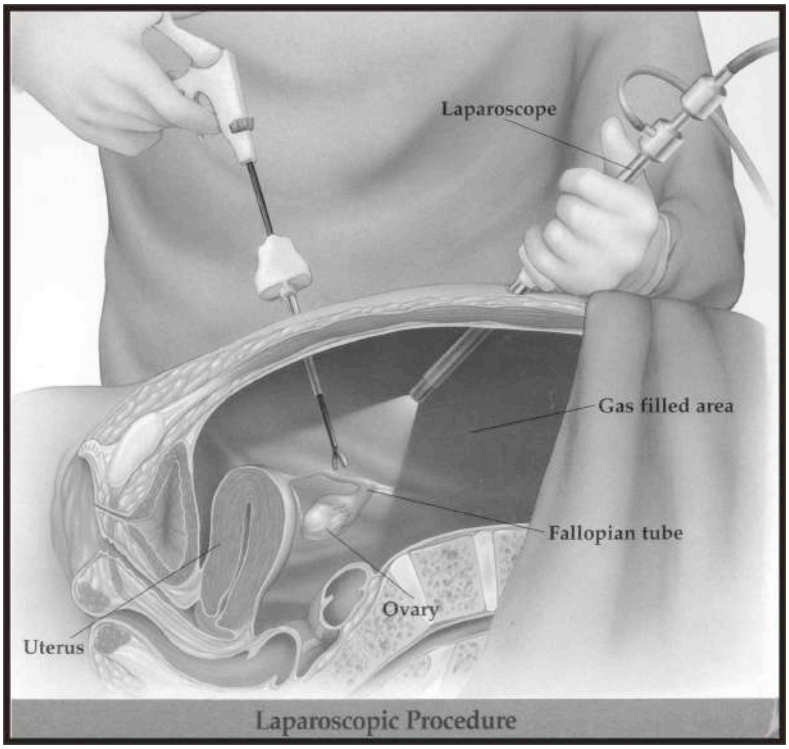
Blood tests and ultrasounds are done in the morning between 8:00 a.m. and ll: 00 a.m. and take approximately 30 minutes. Monitoring is vital and mandatory for safe and effective fertility treatment. If needed, please make arrangements with your employer for scheduled appointments. Although the day is usually predetermined, we try to be flexible regarding the appointment times. Please let the clinical coordinators know what time of morning is best for your visit.

The physician reviews blood results and ultrasounds daily and these are essential to the proper management of your cycle. **Your instructions may not be provided to you by telephone until after 5:30 p.m. Please do not call for results. If you have not received a call by 7:00 p.m., please call the nurse through the Doctor's Directory.** If you will not be at home, let the office know where you will be or where a message can be left. Provide the office with home, work, voice-mail and mobile phone numbers.

❖ LAPAROSCOPY FOR FERTILITY EVALUATION

Laparoscopy is a valuable tool to diagnose and treat many fertility problems, particularly diseases that affect the fallopian tubes or ovaries. Like the hs-HSG or "dye test," laparoscopy may be used to show that the fallopian tubes are open. Unlike the HSG or hs-HSG, laparoscopy can reliably identify adhesions or endometriosis around the ovaries or tubes. Both of these conditions can impair fertility. Thus, laparoscopy remains an essential part of the fertility evaluation. Unless there are concerns from the information you provide, laparoscopy is usually held as one of the final procedures and may be recommended after completion of other basic tests.

Scientific and technical advances now allow specially trained surgeons to correct many conditions without making a large incision (laparotomy) and shortening the recovery time to just a few days. Laparoscopy is a safe and effective way to identify endometriosis and adhesions. Studies now show improved pregnancy rates after corrective laparoscopic surgery. Further, this treatment is usually provided during the same surgery.



❖ DIAGNOSTIC HYSTEROSCOPY IN THE OFFICE SETTING

A diagnostic hysteroscopy is a procedure that allows your doctor to examine the inside of the uterus with a small, lighted scope passed through the cervix. Saline (salt water) is instilled to allow visualization of the uterine cavity. Abnormal conditions of the uterus, such as internal fibroids, scarring, congenital malformations, tumors, polyps and tubal obstruction may be viewed, giving your physician insight on further diagnosis and treatment. Diagnostic hysteroscopy may be completed in the office and is usually scheduled soon after menstrual bleeding has stopped. This office procedure usually takes less than 20 minutes.

Patient Instructions BEFORE Office Hysteroscopy

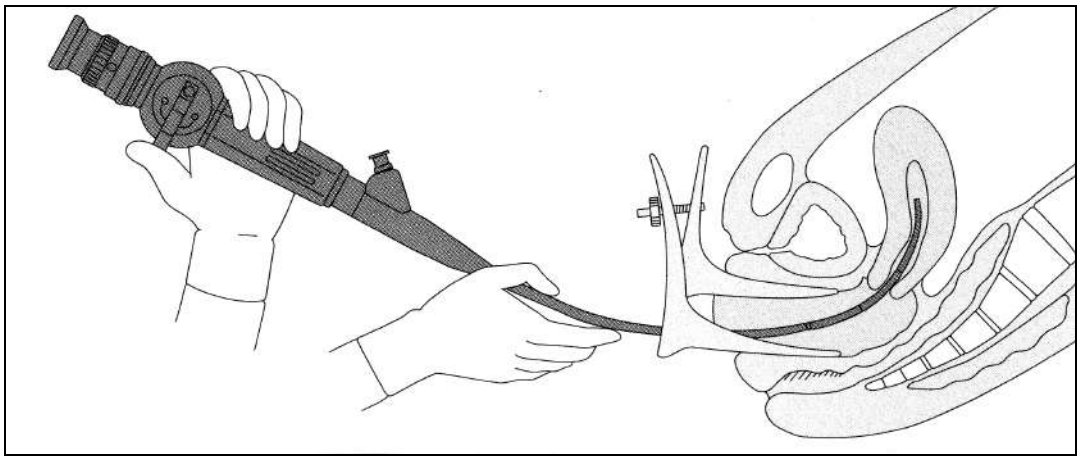
1) Contact the office on day 1 or 2 of your cycle to schedule your surgery. If this occurs on a weekend or holiday, please call the next business day.
2) Take ibuprofen or naproxsyn with a light meal about 1 hour before the procedure

Patient Instructions AFTER Office Hysteroscopy

1. You may experience light to moderate vaginal bleeding for 2 to 6 days. Refrain from intercourse for 2-3 days after the office procedure.
2. Saline is used during the procedure to inflate the uterus. This may cause some discomfort. Take ibuprofen, naproxsyn or Tylenol for pain relief.
3. Call the office immediately if you have any of the following symptoms:

   ◊ Bleeding as heavy as the heaviest flow during your menstrual
   ◊ Severe pain.
   ◊ A temperature of 100.4°F or above.
   ◊ Difficulty urinating.

After office hours, or on weekends or holidays, call the Doctors Directory



FERTILITY MEDICATIONS AND TREATMENTS

❖ ORAL CONTRACEPTIVE PILLS (OCP's)

At first consideration, use of a birth control pill may seem contradictory to achieving pregnancy, but the issue is a bit more intricate. Several situations require alteration of the menstrual cycle to enhance the timing or effectiveness of fertility treatment. OCP's contain a synthetic estrogen and progesterone that temporarily suppress normal ovarian and pituitary hormone production, improving some conditions, such as PCOS and endometriosis. Within the uterus the pills can prevent an abnormal endometrial lining that is out of phase, overgrown or unreceptive to an embryo. When OCP's are stopped, it results in light bleeding, and some women will have no bleeding. Additionally women often have spotting while taking OCP's and this is usually NORMAL! OCP's are <u>always</u> stopped before ovulation drugs are started.

Indications and Benefits

Polycystic Ovary Syndrome (PCOS) - With this condition the ovaries produce abnormal amounts of male hormones and ovulation is often difficult to stimulate. While drugs such as clomiphene and fertility injections sometime induce ovulation, many people are resistant. OCP's improve the PCOS prior to attempting to make the woman ovulate, thus reducing the dose of medicine required.

Persistent Ovarian Cysts - Occasionally a cyst will remain or arise after a natural or stimulated cycle. This would be detected on a "baseline" ultrasound scan and if it is producing hormones, could negatively affect the next cycle. To suppress these types of cysts, OCP's allow time for the cyst to resolve and prevent new ones from developing. Use of OCP's reduces the chance of having to cancel/postpone treatment.

Cycle regulation - Many couples have busy schedules and timing of intercourse is difficult, if not impossible, with their normal menstrual cycle. In such cases, the cycle start may be changed by OCP's, allowing ovulation to fall near a particular date.

Low-responders - Some women produce few follicles and will respond better if given a combination of OCP's and Lupron injections before starting fertility medicines. This appears beneficial to women in their late 30's or 40's.

PATIENT INSTRUCTIONS:

Once you start taking OCP's you should continue until instructed to stop. This is EXTREMELY important when using "Lupron" in combination with OCP's. Please call before stopping the active pills as this might cause a menstrual period and delay your treatment.

SIDE EFFECTS AND RISKS:

♦ Headache, nausea and bloating are uncommon and usually require no change in medication.

♦ **Break-through Bleeding** - Light spotting or bleeding can be an annoying consequence. This may occur at any time and is unpredictable. However, there is no effect on the ovaries and does not usually require any alteration. Call if bleeding exceeds your normal menstrual flow.

♦ **Blood Clots** - With ongoing OCP use (months), the chance of blood clots in leg veins is slightly increased with today's pills, but remains much lower than the risk of clots associated with a pregnancy. If you experience swelling, pain in the legs or shortness of breath, call immediately.

❖ CLOMIPHENE CITRATE

Clomiphene citrate (Clomid®) and femara (Letrozole®) are oral medication used to stimulate ovulation in non-ovulating women. It is also used to enhance the quality of ovulation, to correct luteal phase defects and to ensure the proper timing of artificial inseminations. Clomiphene acts as an anti-estrogen. It "tricks" the pituitary gland into producing more of the hormones that stimulate the ovaries. With clomiphene ovulation, an injection of hCG (Ovidrel®, Pregnyl®) may also be used.

Dosage /Timing The lowest effective dose is desired to avoid side effects. Thickened cervical mucous may occur at higher dosages. Thus, treatment begins with one or two pills a day and is increased as needed. Your physician will determine the dose and the number of days to take clomiphene. Ovulation should occur 5 to 8 days after you take the last tablet. Intercourse or insemination should take place around the time of ovulation. Notify the office when you have a positive LH surge test so that inseminations may be scheduled.

Side Effects (See Risks & Complications section) Common side effects include hot flashes, headaches, breast tenderness, nausea, nervousness, visual disturbances, vaginal dryness and ovarian cysts. Thickened cervical mucous may also occur at higher dosages. Fertility pill treatment increases the rate of multiple pregnancy to 5 - 10%. (Also, see multiple pregnancies)

❖ INJECTABLE FERTILITY MEDICATIONS

Fertility injections are protein hormones, also called "gonadotropins", Follicle Stimulating Hormone (FSH) and Luteinizing Hormone(LH) that are purified from urine of menopausal women or generated in a laboratory. These are administered by intramuscular or sub-cutaneous injection. **Gonal-F®** and **Follistim®** are synthetic FSH made by recombinant DNA technology and are given as sub-cutaneous injections. Bravelle® and Menopur® contain FSH and LH. Gonal-F and Follistim contain only FSH. With injectable fertility medications, ovulation is always triggered by an injection of hCG (Pregnyl®, Ovidrel®) that initiates the release of eggs from the follicle.

Side Effects (See Risks & Complications section)

Mood swings and **pelvic discomfort** may be seen with these medications.

Multiple pregnancy occurs in 20-30% of these cycles when injections are used alone, most are twins.

Ovarian Hyperstimulation Syndrome occurs in less than 1% of cycles. The ovaries may become enlarged and patients can gain five to ten pounds rapidly with severe pelvic pain.

Call the office immediately if you experience any of these symptoms. After office hours, or on weekends or holidays, call the Doctors' Directory.

❖ ASPIRIN 81mg

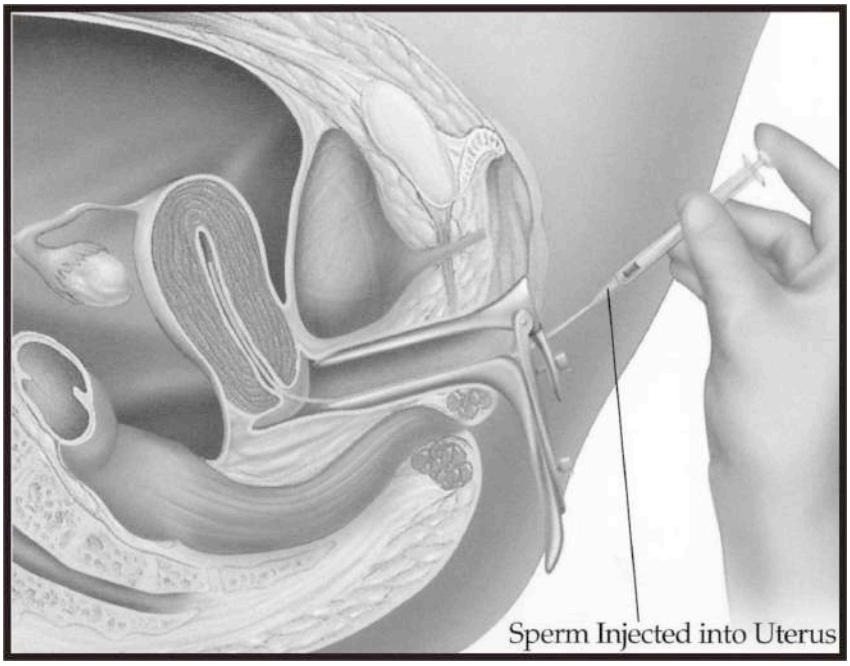
Aspirin may be prescribed to SOME patients undergoing fertility treatment. It is NOT recommended for all patients. Studies have suggested that low-dose aspirin may help to maintain blood flow to the uterus in some circumstances. Recommended dosage is one 81mg tablet per day. This dosage is often called "baby" aspirin. Your doctor will make a recommendation if aspirin may have advantages in your specific case.

❖ MULTIVITAMINS

For general health purposes, it is recommend that all patients take a multivitamin each day. This may be a routine, over-the-counter vitamin. The most important "preconception" component of the vitamin is folic acid (or folate) that has been shown to reduce the risk of a particular type of birth defect, neural tube defects (NTD). All common vitamins contain folate. The double strength of the 'prenatal vitamin' is not routinely needed prior to conception or in the first trimester of pregnancy. There are some concerns regarding over-dosage of some vitamins, e.g. vitamin A and derivatives, such as may occur when prenatal vitamins are taken combination with fortified foods and an otherwise balanced diet.

❖ INTRAUTERINE INSEMINATION (IUI)

Intrauterine insemination (IUI) is a procedure in which sperm are "washed" (concentrated) and placed into the uterus through a catheter. A sperm wash takes about 30 minutes in the Andrology Lab and involves separating the sperm cells from the fluid, white blood cells, prostaglandin's (which can cause uterine cramping) and "debris." In natural intercourse this "washing" is done when sperm swim through the cervical mucus. To place the washed sperm inside the uterus, a speculum is inserted into the vagina and a small catheter connected to a syringe containing the sperm is inserted through the cervix into the uterus. The specimen is injected and the catheter and the speculum are removed (see FIGURE below). The procedure is usually painless and takes only a few minutes. Afterward you should remain reclining for a few minutes.



Patient Instructions

1. A semen specimen for intrauterine insemination should be produced following a two to three day period of sexual abstinence, unless otherwise instructed.
2. Obtain a sterile container from the office to collect the specimen AT HOME !
3. Avoid soaps, detergents, creams or lubricants to aid specimen collection. These agents may interfere with sperm motility. Assistance from the female partner is encouraged and may improve semen quality.
4. Collect the entire specimen in the sterile container. The volume should be between one half and one teaspoon. If there is any spillage, let the lab know.
5. If the specimen is obtained at a location other than the office, it must be delivered to the office/lab as soon as possible (ASAP) after collection. Keep the specimen close to body or room temperature during transportation. **Do not put it near heat or direct sunlight!** Time is not as important as temperature when transporting semen samples, therefore, drive carefully.

6. Always label the specimen cup with your NAME, DATE and TIME of collection and number of days since last ejaculation. According to laboratory policy, specimens received without this information may be refused and may not be processed.

7. Inseminations are scheduled 12-48 hours after +LH surge detected with ovulation kits, or 24-36 hours after administration of hCG.

Side Effects & Risks

Bleeding - You may have some spotting. The cervix is fragile, and insertion of the catheter may cause the tissue to bleed.

Cramping - You may also experience uterine cramping for a short time after IUI and you may take acetomenaphen or ibuprofen.

Infection - Bacteria in the semen or in the vagina may be passed into the uterus with insemination. The chance of infection is believed to be very small but would probably require antibiotics. Although unlikely, a severe infection may require hospitalization and intravenous antibiotics.

Call the local office immediately if you experience any of the following symptoms:

*Cramping that persists or becomes severe.
*Bleeding as heavy as the heaviest flow during your menstrual period.
*A temperature of 100.4˚F or above.

After office hours, or on weekends or holidays, call the Doctors' Directory.

❖ THERAPEUTIC DONOR INSEMINATION (TDI)

Despite great advances in treatment of male factor infertility, there is occasionally a need for donated semen. Use of donor sperm may be indicated when there is absence of sperm or the available sperm cannot fertilize eggs. The success of insemination with thawed, frozen, donor sperm appears to be somewhat lower than the chance of conceiving with fresh sperm.

Several national sperm banks recruit and screen donors according to standards established by the American Society for Reproductive Medicine (formerly called American Fertility Society) and the American Association of Tissue Banks. The genetic and medical histories of each donor, as reported by the donor, are reviewed and traced back two generations. The donor and his sperm are screened for some, but not all genetic diseases such as sickle cell anemia, Tay-Sachs disease, thalassemia, and for various sexually transmitted diseases, including but not limited to hepatitis, human immunodeficiency virus (HIV), cytomegalovirus, gonorrhea, chlamydia, trichomonas, monilia, gardnerella and syphilis. These standards have been established to reduce the risk of transmission of genetic and infectious diseases. However, in spite of these precautions, it is possible for donated sperm to harbor unidentified genetic abnormalities or undetected infections which may be passed on to the resulting child(ren). Infected sperm may also pass on a disease to the woman attempting pregnancy.

The risk of major birth defects following use of donor sperm appears to be the same as in the general population. Similarly, there is no apparent increase in the risk of pregnancy complication following donor sperm insemination.

Before starting a treatment cycle, the woman/couple may be provided with a list of several sperm banks and information on how to inquire about donor sperm. It is the responsibility of the woman/couple to select and contact the sperm bank, select the donor and order the sperm of their choice, and ensure its timely delivery to this facility for analysis and preparation for insemination.

When use of donor sperm is indicated, it is strongly recommended that the couple participate in at least one counseling session with a local psychologist or licensed counselor. This may be waived if the couple acknowledges the concerns and declines this request. NewLIFE does not participate in inseminations from a "known" sperm donor, relative or friend.

If elected, both female recipient and partner/spouse (if applicable) will be asked to provide consent on a separate form for use of sperm from a donor bank. You will be authorizing this practice to use sperm from a single donor as the sole source of sperm in a treatment cycle(s) and that, from the moment of insemination, you accept any child(ren) resulting from the procedure of donor sperm insemination as your own. The child(ren) produced as a result of donor sperm insemination is/are considered, in all respects, the child(ren) of the woman/couple. Financial responsibility for the pregnancy, any pregnancy complications and the child(ren) resulting from donor sperm insemination, is the responsibility of the woman/couple.

SIDE EFFECTS, RISKS AND COMPLICATIONS OF FERTILITY TREATMENT

❖ OVULATION INDUCTION MEDICATIONS

Overall, side effects directly due to fertility medications are uncommon and mild. For patient education purposes some of these are described in this section of the booklet.

The most frequent adverse reactions to clomiphene include ovarian enlargement, transient hot flushes (which may be unpleasant but are not dangerous) and abdominal discomfort. Women who do not ovulate normally on their own, may notice new symptoms usually associated with ovulation, e.g. mid cycle ovulation pain, premenstrual symptoms (abdominal discomfort, breast tenderness, etc.) and menstrual cramps. If you experience persistent or progressive pelvic pain, you should report it to your physician. Other side effects, occurring in a very small percentage of women, include nausea, vomiting, nervousness, insomnia, visual symptoms, headache, dizziness and light-headedness.

Fertility injections are protein hormones similar to, and with some, identical to those made in the body. Thus, side effects are uncommon. The chance of multiple pregnancy (e.g. twins, triplets, etc.) with injections is significantly increased (See Multiple Pregnancy page that follows). Most of the side effects of these drugs are minor, involving discomfort, but not usually requiring ongoing or unusual medical intervention. The manufacturers advise that rare but serious pulmonary conditions and thromboembolic (blood clot) events have been reported in conjunction with the use of ovarian stimulation medication and some patients might have a hypersensitivity (allergy) to such drugs. Symptoms of generalized rash, swelling or difficulty breathing should be reported immediately to your doctor.

These 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 removed surgically, in which case hospitalization may be required. It is also possible for ovarian cysts to rupture, causing an 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. The removal of an ovarian cyst can result in the loss of an ovary, though this is uncommon.

Though it is recommended to avoid use of any medications during pregnancy, it is 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 starting treatment. Additionally, couples may be asked to refrain from intercourse, or use barrier protection at certain times of the woman's cycle.

❖ ECTOPIC PREGNANCY & WARNING SIGNS

An **ectopic pregnancy** is a pregnancy that implants somewhere outside of the uterus. It can occur in a fallopian tube, on an ovary, or in rare instances inside the cervix or in the abdomen. The pregnancy does not usually develop normally and may rupture, causing bleeding and damage to the tube or ovary. **If not treated it can be life threatening.**

Ectopic pregnancy occurs in less than l% of pregnancies. Women with a history of prior ectopic pregnancy, chlamydia, pelvic inflammatory disease, gonorrhea, endometriosis and/or tubal adhesions are at higher risk. Diagnosis of an ectopic pregnancy is usually made with ultrasounds and blood hormone studies. In some instances the drug methotrexate can be used to treat the condition or surgery may be required to remove the pregnancy.

Symptoms of an ectopic pregnancy may include:

* Uterine cramping/bleeding
* Sharp lower abdominal pain on the right or left side.
* Light-headedness or fainting
* Cold sweats
* Shoulder pain

Infertility patients have an increased risk for an ectopic pregnancy. Therefore, your blood hormone levels will be monitored and an ultrasound scheduled early in pregnancy to rule out an ectopic pregnancy. **Call the office immediately if you experience any of the symptoms listed above.** After office hours, or on weekends or holidays, call the Doctors Directory.

❖ OVARIAN HYPERSTIMULATION SYNDROME

Ovarian Hyperstimulation Syndrome (OHSS) is a serious condition that results from an exaggerated response to fertility medications used for ovulation induction. It typically arises after ovulation (hCG injection) and is more likely if a pregnancy occurs. When it develops, ovaries may become too large and may leak fluid, bleed, twist or rupture. Fluid may collect in the abdomen and/or lungs and blood may become concentrated resulting in kidney damage or blood clots, if not treated. Severe ovarian hyperstimulation is rare (<1%) in patients closely monitored but women with polycystic ovary syndrome and those that conceive are at higher risk.

OHSS is best managed by prevention and close cycle monitoring with ultrasound and blood tests. Use of large volumes (2 liters/day) of electrolyte containing fluids (Gatorade®, Powerade®) may be advised in some cases, and if unable to tolerate oral fluids, intravenous replacement may be needed. If an exaggerated response occurs, the cycle may be canceled by withholding the hCG injection and avoiding intercourse. Birth control pills may also be used to reduce the cyst size.

Once OHSS develops it is most commonly improved by removal of excess fluid in the abdomen, but may also respond to or be managed with intravenous fluid therapy, salt restriction, albumin and avoidance of abdominal and pelvic exams and intercourse. These therapies will sometimes require hospitalization when potentially life-threatening conditions arise.

Symptoms

- Persistent pelvic pain
- Abdominal fullness
- Difficulty breathing
- Decreased urination
- Rapid weight gain (2 lbs or more per day)
- Nausea/vomiting
- Diarrhea

If you develop any of these symptoms during the 1-4 weeks after the hCG injection, contact the office immediately. After hours or on holidays call the Doctors Directory.

❖ MULTIPLE PREGNANCIES

Multiple pregnancies / multiple births: As fertility medications may stimulate more than one egg (often that is the primary goal), pregnancy with two or more babies occurs more often than the 1-2% of spontaneously conceived pregnancies in the general population. Multiple pregnancies occur in about 7% of clomiphene stimulated cycles and 20-30% if fertility injection cycles. The majority of pregnancies in both cases are twins.

Unfortunately, multiple pregnancy cannot be reliably predicted or prevented. Mothers carrying multiple pregnancies are at higher risk of anemia, pregnancy-induced hypertension (toxemia), liver dysfunction, bleeding, infection and early labor with ruptured membranes. Serious maternal complications increase, in general, with each additional gestation as shown in Table 1.

Table 1. Rates of Major Maternal Complications by Fetal Number

Number of Fetuses	Preterm Labor	Preterm Delivery	Gestational Diabetes	Pre-eclampsia
1	15%	10%	3%	6%
2	40%	50%	5-8%	10-12%
3	75%	92%	7%	25-60%
4	>95%	>95%	>10%	>60%

Source: American Society for Reproductive Medicine. Practice Committee Report. Nov 2000

Most pregnancies will require C-section delivery. Medical conditions in the mother will further raise the risk for maternal complications. Babies from multiple pregnancies have a higher risk for miscarriage, abnormal growth, birth defects and genetic abnormalities and handicaps due to prematurity and early delivery. Premature delivery is common in twins and expected in pregnancies with three or more babies. The risk to premature infants increases the earlier they are born and the possibility for severe complications with potential life-long disabilities exist. Pediatric intensive care for multiple premature babies is very expensive and many couples express deep concern about caring and raising multiple children at the same age.

When considering the possibility of these obstetrical and neonatal complications, couples may consider selective reduction to twins or singleton pregnancies. A couple's attitude toward this procedure should be considered BEFORE initiation of fertility treatment. A couple having serious emotional, ethical, or religious reservations regarding the selective reduction procedure may wish to limit the risk in a number of ways. Options include: a)

cancel any stimulated cycle with more than 3 mature follicles; b) substitute sexual intercourse for insemination; c) convert the cycle to In Vitro Fertilization where the number of embryos placed into the uterus may be controlled. Not all of these options are absolutely secure.

Should three or more viable pregnancies be confirmed by ultrasound, you will be offered counseling regarding obstetrical outcome and interventions such as multi-fetal pregnancy reduction ("selective reduction"). These are extremely difficult issues for all couples. Please discuss this with your partner first and then with your physician BEFORE consent forms are signed and before treatment begins. Hopefully this situation will not arise, but you should discuss this issue as a couple and be in agreement on a plan of management.

❖ MULTIFETAL PREGNANCY SELECTIVE REDUCTION

Though a very difficult decision, and not an option for all couples, reducing a multiple pregnancy to twins or triplets is available at large medical referral centers around the country. The method used is effective and safe. The chance of endangering the entire pregnancy is low (4-9%) but this risk is increased when larger numbers of pregnancies are reduced (i.e. quintuplets versus quadruplets).

Though pregnancies reduced to twins and triplets retain the possibility for pregnancy complications, reduced pregnancies will have significantly better outcomes than those not reduced as the length of pregnancy and birth weight of the babies are increased, reducing the chance of long term disabilities.

To address this difficult situation, couples should discuss this issue and decide together what their choices would be in such cases. Their decision may be aided by consultation with clergy, a perinatologist (high-risk pregnancy specialist) and other counselors.

❖ PREGNANCY AND BIRTH FOLLOWING FERTILITY TREATMENT

The likelihood that infertility treatments will result in a pregnancy or live birth depends on many individual factors: primarily, the age of the woman, the quality of the sperm, the response of the woman's ovaries to stimulation with clomiphene or gonadotropins, the underlying cause(s) of infertility, and the condition of the uterus. Whatever the course of treatment, the response of any individual patient cannot be predicted with certainty. It is important to discuss your particular circumstances and history with your physician in order to arrive at a reasonable understanding of your chances of pregnancy or birth following on or more treatment cycles. However, there are no guarantees of successful outcome no matter how favorable the rate projected for a given couple.

After pregnancy is achieved, the following complications may occur:

1. The fetus may not develop normally and spontaneous miscarriage may occur.
2. Abnormalities in the fetus become suspected or detected through prenatal diagnostic procedures (e.g. "triple screen" blood testing, chorionic villus sampling, amniocentesis or ultrasound) and may lead the woman/couple to decide to terminate the pregnancy.

Even an apparently normal ongoing pregnancy presents risks to both the mother and the baby, and cannot guarantee a normal delivery at term of a healthy infant. In pregnancies occurring after infertility treatments, as in pregnancies resulting from intercourse, serious unforeseen obstetrical complications occur. Such complications may result in miscarriage, the loss of the child in advanced pregnancy (stillbirth) or delivery of a baby too premature to survive. A prematurely born infant may experience serious life threatening complications or permanent medical disability.

While the use of medications for ovulation induction involves increased risk of multiple pregnancy, other obstetrical complications (not related to multiple birth) seem to occur following infertility treatments at the same rate that they occur in pregnancies following spontaneous conception.

The rate of major birth defects in children born to mothers in the general population is about 3-4%. The risk that a child will be born with a major birth defect increases as its parents' ages increase. There is no evidence that genetic problems, which are responsible for half of birth defects, are increased by infertility treatments. But amniocentesis and/or chorionic villas sampling, each of which can aid the recognition of many of these defects early in pregnancy, should be discussed with your obstetrician. Ultrasound screening and other examinations may detect some but certainly not all defects. It is generally recommended that women who will be age 35 years or older by the date of expected delivery should consider prenatal diagnostic testing. This should be discussed with your obstetrician.

In rare instances, pregnancy may result in serious harm or even death to the mother due to occurrences such as pulmonary embolism (blood clot to the lung), stroke to hemorrhage after delivery. There is no known increased risk for these complications in pregnancies following infertility treatments.

The Reproductive Endocrinology and Infertility physicians do not function as obstetricians, but will work cooperatively with a woman's obstetrician in early pregnancy. Generally, the diagnosis and early care of pregnancy are provided by the specialist, but the patient returns to her obstetrician for routine care after a healthy pregnancy has been established, usually around the 7-8th week. Details of her infertility treatment, the pregnancy hormonal testing and pregnancy ultrasound scans will be released to the obstetrician designated by the woman/couple and to the referring physician, unless specifically requested otherwise by the woman/couple.

❖ OVARIAN CANCER RISK

The risk of ovarian cancer appears to be related in part to the number of times a woman ovulates and also to her number of pregnancies. Infertility alone increases a woman's lifetime risk of ovarian cancer; birth control pill use decreases this risk. In November of 1992, a published study suggested a potential risk of ovarian cancer associated with the use of certain medications for ovarian stimulation. Studies have since supported and refuted the elevated risk and the consensus of medical opinion on the issue, as voiced by the Society of Assisted Reproductive Technology (SART) and the American Society of Reproductive Medicine (formerly the American Fertility Society), is that there is no conclusive evidence of risk. In the 2000 ASRM Patient Information Series, a booklet titled "Ovulation Drugs", states that it is not known whether fertility drugs cause an increased risk. In fact, in one well-known study, the achievement of pregnancy with or without the use of infertility drugs was associated with the decreased ovarian cancer risk. Clearly, more research needs to be conducted to address these issues. In the meantime, it is important that women taking these medications discuss the risks with their physicians. One must weigh the unproven risks against the clear benefits of ovulation-inducing agents.

Until further information is available through carefully controlled studies, continued, but cautious use of these medications is reasonable as pregnancy and breast-feeding reduce a woman's risk. One recommendation has been to optimize the chance of conception in any cycles in which these medications are utilized. This is best done by completing an infertility evaluation before initiating ovulation induction and by use of oral contraceptive pills when a woman is not a woman is not seeking pregnancy. Nevertheless, recipients of fertility medications should be aware of the possible increase in ovarian cancer risk and may discuss this issue with your physician and review the ASRM Patient Fact Sheet for this topic.

PATIENT CONSENTS TO FERTILITY TESTING AND TREATMENT

Hysterosalpingography (HSG or "dye test") is a diagnostic test to determine if the fallopian tubes are open, providing sperm an access to the egg. Pictures are made with X-ray after the uterus is filled by "dye" or with ultrasound after filling with salt water (saline). Uterine cramping is common during this short, but important test. Infection may occur in less than 1% of patients but may require hospitalization and intravenous antibiotics. There are no simple alternatives to obtain this vital fertility information.

Hysteroscopy and **hysteroscopic hysterogram (hs-HSG)** are office procedures to view the inside of the uterus for defects or abnormalities (fibroids, polyps, adhesions) that may interfere with embryo implantation or normal pregnancy, and confirm tubal patency, respectively. Salt water is used to fill the uterus and a thin flexible instrument is passed through the cervix to display an image. There may be some mild cramping during the procedure and although rare, infection and perforation of the uterus are possible complications.

Ovulation induction is performed with clomiphene citrate (Clomid®, Letrozole®) and/or Human Menopausal Gonadotropins or synthetically prepared FSH hormone (hMG, Gonal f®, Follistim®). Clomiphene and Letrozole® are given orally and may require blood testing. Although currently used by physicians for infertility treatment, Letrozole and some other medications are only FDA approved for uses other than fertility. Fertility injections are used to stimulate more than one egg per cycle and require daily injections for an average of 10 days. Blood hormone levels and ovarian ultrasounds must be performed to monitory your response and will be performed every 2-3 days while taking the injections. When the eggs are ready to ovulate (mature), a different injection, human chorionic gonadotropin (hCG) will be given to stimulate the release of your eggs. If pregnancy is suggested by a missed period and confirmed by blood tests, ultrasound may confirm the location of the pregnancy.

Possible Risks and Discomforts:
This therapy is associated with possible risks from drawing blood samples and ovarian examination by ultrasound and use of fertility medications and injections. Treatment may be cancelled for over- or under-stimulation or if patients are unable to comply with safe monitoring.

Risks of Drawing Blood Samples

a) Discomfort, bruising (leaking of blood into adjacent tissue) and bleeding from the puncture site occur with moderate frequency, are usually not serious and have no long-term effect. These discomforts may be treated by direct pressure and by applying moist heat.

b) Infection may occur following puncture of the skin by the needle. The chance that this will occur is very low and no serious harm will result. Treatment is with antibiotics and moist heat.

c) Anemia may result from the drawing of large amounts of blood. Because so little blood is drawn for this therapy (no more than 100cc per month), the chance that anemia will occur is very low, and correction of any blood loss should be easily accomplished by the iron in your diet.

Complications and Risks of Fertility Injections and hCG Injections

a) Injury from injection: You, your partner or another individual may be trained to give the injections. There is some risk that damage may occur from the needle in the skin or muscle. Deep injections may cause nerve injury and subsequent pain and numbness. There is no treatment and symptoms from the nerve injury may go away without treatment.

b) Allergic reactions: These are rare but usually consist of skin rashes, dizziness or pain at the injection site. Symptoms may be treated with an antihistamine or other medications.

c) Emotional changes: Moodiness, anxiety and irritation are possible but usually require no treatment.

d) Ovarian Hyperstimulation (OHSS): Severe ovarian hyperstimulation is rare (<1%) for patients closely monitored but women with polycystic ovary syndrome and those that conceive are at higher risk. If over-responsive to fertility medications, your ovaries may become too large, may bleed, twist or rupture. Fluid may collect in your abdomen and/or lungs and your blood may become concentrated resulting in kidney damage or risk for blood clots. Hyperstimulation is often treated with intravenous fluid therapy, salt restriction, protein infusions, removal of abdominal fluid and careful avoidance of abdominal / pelvic exams and intercourse. It may require hospitalization that may not be covered by insurance. OHSS is best avoided by withholding hCG injection and avoiding pregnancy in hyper-responsive cycles.

e) Multiple pregnancies / multiple births: Because these medications may stimulate more than one egg, pregnancy with two or more babies occurs in up to 25% of pregnancies versus 1-2% in the general population. This cannot be reliably predicted or prevented by contemporary monitoring but poses higher risks for miscarriage, infant abnormalities, pregnancy induced hypertension (toxemia), hemorrhage, premature delivery and handicaps due to low birth weight along with other maternal complications. In

addition, care for multiple, premature babies is very expensive and demanding. Options such as selective reduction and others have been presented in sufficient detail.

f) Miscarriage & Ectopic (tubal) Pregnancies: Pregnancy after fertility injections is associated with a risk of miscarriage of 20-25% and is similar to the rate seen in infertile women in general. While ectopics occur in <1% of pregnancies, these treatments and being infertile may carry a slightly higher risk of 1-3%. Tubal pregnancy might require surgery or medicines. Combinations of tubal and intrauterine pregnancies (heterotopic) require surgical treatment.

g) Ovarian Cancer: Risk of ovarian cancer appears partly related to the number of times a woman ovulates and carries a pregnancy. Infertility alone increases this risk, while pregnancy and birth control pill use decrease risk. Controversial and contradictory reports of a possible link between fertility drugs and ovarian cancer have been published. Until further studies are completed, careful, but continued use of these medications is reasonable as pregnancy and breastfeeding reduce cancer risk. Potential recipients of fertility medications should be aware of the possibility of increased risk of ovarian cancer.

Intrauterine Insemination (IUI) is a procedure for placement of sperm inside the uterus. If IUI has been recommended in place of sexual intercourse, the male partner will be asked to provide a semen sample to our office lab after the female receives the hCG injection. Semen is prepared to separate sperm from seminal fluid and concentrate the most motile sperm.

Risks of Intrauterine Insemination (IUI)

a) Uterine cramping occurs with moderate frequency during and after insemination but is usually mild and of short duration. Treatment is usually not required.

b) Infection. Bacteria in the semen or in the vagina may be passed into the uterus with insemination. The chance of infection is believed to be very small but would probably require antibiotics. Although unlikely, a severe infection may require hospitalization and intravenous antibiotics.

INFORMED CONSENT: With knowledge and recognition of the above risks, I/we hereby consent to diagnostic testing and if recommended, diagnostic/therapeutic procedures with ovulation inducing medications and insemination. I/we have received the Patient Information Booklet and counseling provided by healthcare professionals. Specifically, though not exclusively, the risks of ovarian hyperstimulation, multiple births, and long-term risks of ovarian cancer have been explained to me/us. Furthermore, I/we hereby confirm understanding of the need to follow carefully the recommended dosages of self-administered medications and that I/we agree to continue to return for evaluation and care as long as these medications are prescribed. I/we am/are aware that an office staff member is available for consultation for my/our questions and concerns and that no guarantee of outcome has been offered. I/we hereby acknowledge that I/we have been given the opportunity to inquire about the potential risks and side effects of these medications and treatments, and that I/we recognize my/our right to refuse any therapy. My/our questions regarding fertility medications and treatments have been satisfactorily answered and I/we hereby provide fully informed consent.

Female's Signature: _____ **Date** _____

Male's/Partner's Signature: _____ **Date** _____

Witness of Identification and signature _____