



DIAGNOSTIC TESTING SECTION

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OVERVIEW OF THE HUMAN REPRODUCTIVE SYSTEM

Proper functioning of both the female and male reproductive systems requires the interaction of various organs of the human body. The reproductive process begins in the portion of the brain known as the hypothalamus where the hormone GnRH (gonadotropin releasing hormone) is produced. GnRH is chemically transmitted via the bloodstream to the pituitary gland, where it stimulates the production of the two hormones known as Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH). These two hormones migrate to the respective human reproductive organs (testes, ovaries) where they serve various functions such as ovulation induction in the female, sperm production in the male, and production of sex hormones in each.

THE FEMALE

Follicles are fluid-filled sacs located within the ovary, which contain an egg (oocyte). Follicular development in the ovaries commences via hormonal stimulation provided for by the aforementioned FSH. As these follicles grow, other cells found within them, known as granulosa cells, begin to produce the female sex hormone estrogen. Following a series of complex hormonal events, one follicle will assert itself as the “dominant follicle” by the eighth day of the menstrual cycle. From this point onward, only the dominant follicle will mature in response to continuous FSH stimulation. All other follicles will begin to regress through a process known as atresia. (Each ovary has an equal probability of producing the dominant follicle each month. Over time, half of the dominant follicles would be expected to occur on the right ovary, and half on the left. It is a rare occurrence for follicular development to alternate ovaries from cycle to cycle.)

As the growth of the dominant follicle progresses more estrogen is produced. Additionally, this continuous growth allows the oocyte located inside the dominant follicle to continue maturation. Once the estrogen secreted by the granulosa cells of the dominant follicle reaches an elevated level for 2-3 consecutive days, the pituitary gland responds by producing a surge of LH. This phenomenon, known as the LH surge induces ovulation.

Ovulation is defined as the release of the oocyte from the follicle. Once ovulation occurs, the oocyte is picked up by the four inch long fallopian tube. This structure is connected to the uterus at one end, and the fimbria at the other. The fimbria consists of delicate finger-like projections which sweep over the surface of the ovary, and move the oocyte into the fallopian tube. The oocyte is propelled along the fallopian tube toward the uterus by tiny hair-like cilia. After release of the oocyte from the dominant follicle, the follicle seals over and becomes a corpus luteum, the main function of which is the production of the hormone progesterone. The development of a successful pregnancy relies heavily upon the production of progesterone by the corpus luteum.

When intercourse occurs, sperm are deposited in the vagina, where they swim through the cervix into the uterine cavity, and out into the fallopian tubes where fertilization may occur. Although millions of sperm are usually deposited in the vagina with each ejaculation, only several hundred are able to complete the journey to the fallopian tube, due to the numerous barriers encountered along the way. The most important of these barriers, the cervical mucus, undergoes changes at midcycle in response to estrogen secreted by the dominant follicle. These changes in turn enable sperm to pass through the mucus and into the uterine cavity.

Following ovulation, the oocyte is capable of fertilization for approximately 12-24 hours, whereas sperm are capable of fertilizing an oocyte for up to 24-48 hours. If fertilization does not occur during this relatively brief period, the egg and sperm will die. If fertilization does occur, the resultant embryo will continue its journey through the fallopian tube into the uterine cavity. Approximately 5-7 days after fertilization, the embryo will implant on the uterine wall, and if it continues to grow will result in a viable pregnancy. Occasionally, the embryo implants within the fallopian tube, a condition known as an ectopic pregnancy. If left untreated, this condition may result in the rupture of the fallopian tube, a life-threatening emergency.

A resulting embryo secretes a hormone, known as human chorionic gonadotropin (hCG). This hCG stimulates the corpus luteum to continue making progesterone until the embryo is mature enough to continue progesterone production itself (after approximately 12 weeks of gestation). Due to continued progesterone production by the corpus luteum, the endometrium continues to grow, and no menstrual period will occur.

If pregnancy does not result, then 12-24 days after ovulation, the corpus luteum will stop producing progesterone altogether. The uterine lining, or endometrium as it is otherwise known, will shed from the uterine wall over the course of several days. This is known as the menstrual period.

THE MALE

Once FSH reaches the testicle, it stimulates the production and maturation of millions of sperm on a daily basis. The testicles are also responsible for the production of the male sex hormone testosterone.

Once sperm are produced, they are secreted into a series of tubular structures within the testicle where they mature for approximately 70-80 days. Following this seemingly lengthy period, sperm are then secreted into the respective testicular structures of the epididymis and vas deferens, where they will undergo further maturation, lasting an additional 10-14 days.

Although sperm have undergone extensive maturation within the male reproductive tract, they are not yet capable of fertilizing an oocyte, as additional maturation of sperm must occur within the female reproductive system. These processes of additional maturation in the female reproductive tract are known as capacitation and the acrosome reaction. Capacitation involves a poorly-defined series of enzymatic reactions, which lead to the acrosome reaction. The acrosome reaction alters the cap that covers the head of the sperm. When the cap is altered, enzymes on the surface of the sperm head are exposed and activated to break down the membranes surrounding the oocyte, allowing the sperm to penetrate the egg.

BLOOD TESTS

Your physician may order the following blood tests based on information gathered from your individual medical history. Certain blood tests are requirements and others are recommendations of both our clinic and The American Society for Reproductive Medicine for participation in our IVF programs.

ABO/ RH: commonly referred to as “blood type”; ABO refers to one of four blood groups (A, B, AB, or O), and RH refers to the Rhesus factor (a blood group antigen) in the blood (positive or negative).

RH-negative pregnant women with RH-positive partners may carry RH-positive fetuses. Fetal cells may cross the placenta to the mother and cause production of antibodies in the maternal blood. These resultant maternal antibodies may in turn cross back through the placenta and into the fetal circulation causing destruction of fetal blood cells. This series of events may then trigger reactions ranging from anemia to fetal death in utero. This potentially serious condition can be easily prevented if RH-negative pregnant women receive Rhogam injections.

Antibody Screen: a test used to measure the presence of antibodies and red blood cells in the blood.

Anticardiolipin Antibody: similar to lupus anticoagulant, this antibody may be found in patients with recurrent pregnancy loss.

Antinuclear Antibody (ANA): a test used to diagnose patterns associated with certain autoimmune diseases.

Antisperm Antibody: tests for antibodies that bind to sperm and may reduce fertility.

BUN: evaluates kidney function.

CBC: to determine general health status and to screen for a variety of disorders.

Chlamydia: to screen for or diagnose a chlamydia infection.

Creatinine: to determine if your kidneys are functioning normally.

Cystic fibrosis: to determine whether a person carries the gene for cystic fibrosis. Testing is offered to 1) adults with a positive family history of CF, 2) partners of people with CF, 3) couples currently planning a pregnancy, 4) couples seeking prenatal testing.

DHEA-S: a hormone that is measured in order to identify the source of excessive androgen in women who do not have regular menstrual cycles and/or have excessive body hair.

Electrolytes: to detect a problem with the body's electrolyte balance. Used in routine health screening, or when your doctor suspects that you have an excess or deficit of one of the electrolytes (usually sodium or potassium), or if your doctor suspects an acid imbalance.

Estradiol (E2): an ovarian estrogen that is measured periodically throughout the process of ovarian stimulation in order to determine the appropriate time to induce ovulation; it is also measured along with other hormones in order to evaluate ovarian function or reserve.

Follicle Stimulating Hormone (FSH): a pituitary hormone that stimulates egg maturation in the ovaries; the level is usually measured in conjunction with the hormones estradiol and LH on Day 3 of the menstrual cycle in order to evaluate ovarian function or reserve; high levels suggest premature ovarian failure, low levels suggest hypothalamic pituitary failure; altered FSH/LH ratio may indicate polycystic ovarian syndrome.

GC culture: to screen for *Neisseria gonorrhoeae*, which causes the sexually transmitted disease gonorrhea.

Glucose: to determine whether or not your blood glucose level is within normal ranges; to screen for, diagnose, and monitor **diabetes, pre-diabetes,** and hypoglycemia (low blood glucose).

Hemoglobin (Hgb): the main component of red blood cells; low levels may indicate diseases associated with anemia; high levels while undergoing infertility treatment may indicate ovarian hyperstimulation syndrome (OHSS).

Hepatitis B Antigen: screens for the infectious disease Hepatitis B; if positive, it indicates previous exposure to Hepatitis B, but does not necessarily imply active Hepatitis B infection

Hepatitis C Antibody: screens for the infectious disease Hepatitis C; if positive, it indicates previous exposure to Hepatitis C, but does not necessarily imply active Hepatitis C infection.

Human Chorionic Gonadotropin (HCG): levels of this hormone provide the most sensitive and specific measurement for the detection of early pregnancy.

Human Immunodeficiency Virus (HIV) Antibody: screens for the infectious diseases HIV Type 1 and HIV Type 2 which are the viruses commonly referred to as AIDS; a positive test result does not necessarily imply active AIDS infection.

Human T-Cell Lymphotropic Virus (HTLV) Antibody: screens for the infectious diseases HTLV Type I and HTLV Type II, which are retroviruses associated with adult T-cell leukemia and demyelinating neurologic disorders; a positive test result does not imply active infection, nor does it suggest infection with HIV or a risk of developing AIDS.

17-Hydroxyprogesterone (17-OHP): to help evaluate insulin production and to determine if your insulin is either being inappropriately released or utilized by your body (used to screen for insulin resistance often associated with PCOS).

Karyotyping: to 1) determine whether the chromosomes of an adult have an abnormality that can be passed on to a child, 2) determine whether a chromosome defect is preventing a woman

from becoming pregnant or causing her to miscarry, 3) determine whether a chromosome defect is present in a fetus or infant, 4) to determine whether chromosomal problems may have caused a fetus to be stillborn, 5) determine the cause of a child's birth defects or disability

Lupus anticoagulant: a test in which positive results may be indicative of an increased risk for spontaneous miscarriage.

Luteinizing Hormone (LH): a hormone that is measured in conjunction with FSH in order to determine ovarian function or reserve; it also predicts in advance when ovulation is occurring.

Progesterone (P4): a hormone produced by the ovaries sometimes measured in order to determine whether or not ovulation has occurred; also functions to prepare the uterine lining for possible implantation of a fertilized egg. With pregnancy, it continues to nourish the lining.

Prolactin: a pituitary hormone that if elevated, could cause a milky discharge from the breast, cessation of menstrual periods, and infertility.

This test is performed on a FASTING a.m. blood sample: NO food or fluids (except water) after midnight the evening preceding the test; also, avoid any breast/nipple stimulation for 24 hours prior to the test.

RPR: to diagnose infection with syphilis in sexually active persons. Pregnant women also are screened, and many states in the U.S. require a blood test for syphilis when applying for a marriage license to prevent the spread of infection to others, especially a newborn baby.

Rubella Antibody: an adequate titer of this antibody will establish whether or not an exposure to German measles and/or vaccination for the disease has occurred.

The rubella virus causes a contagious disease characterized by fever and rash commonly referred to as German Measles, and, if acquired by a pregnant female during the first trimester of pregnancy may cause congenital fetal abnormalities, miscarriage, and stillbirth. Due to these serious and potentially devastating consequences, it is highly recommended that women who are not immune do receive the vaccine. Since the vaccine is a live virus, a woman MUST contracept for 1 month following the injection. If a patient's rubella status is "not immune" and she chooses not be vaccinated, she must sign a waiver deferring the vaccine and may then proceed with treatment.

Semen culture: checks for bacteria that may cause genital infection.

Testosterone: a hormone secreted by the adrenal glands and mostly the ovaries; useful in the detection of adrenal or ovarian tumors and virilization in women; elevated levels of this hormone are associated with female masculinization, polycystic ovaries, and excessive virilization.

Thyroid Stimulating Hormone (TSH): a hormone that is measured to assess thyroid function, and/or to evaluate progress of thyroid hormone replacement therapy.

Ureaplasma Culture – to detect the presents of Ureaplasma Urealyticum, a bacterial infection, often present in women who experience infertility with recurrent pregnancy loss.

PRESCREENING PROCESS

- ❖ **Prescreening (IVF)** – As directed by RMIA’s physician, a couple may go directly to the prescreening process (general testing). Prescreening is a series of tests to determine if the couple is an appropriate candidate for IVF. Some of the tests must be preformed though RMIA or a specific laboratory to comply with FDA regulations and for consistent lab values. The following are some of the tests that have specific requirements on where they need to be done.
 - **Infectious disease testing** – all infectious disease testing must be processed through Memorial Blood Centers. Couples can have their blood drawn at RMIA or at their local clinic and then send the kit to Memorial Blood Center for testing. RMIA will provide patients with an infectious disease testing kit and instructions if needed. RMIA is responsible for billing the couple’s insurance for those infectious disease tests.
 - **Day 3 labs** – all day 3 labs (E2, FSH and LH) must be processed at RMIA. A kit can be mailed to patients living out of the Twin Cities area. The patient will be billed for the shipping costs.
 - **Semen Analysis** – is the most comprehensive test preformed for male infertility. It consists of several different individual components: volume, pH, viscosity, appearance, motility, agglutination, progression, concentration, and morphology. This test must be performed at RMIA.

IMPORTANT NOTE: Andrology Services fall under our non-participating company Infertility Laboratory & Surgery Center Associates (ILSCA) which does not participate with any insurance carriers. The semen analysis will need to be paid for on the day of the collection. The cost of the semen analysis is \$110. A claim for the semen analysis will be submitted on the patient’s behalf to their insurance carrier.

2101 Woodwinds Dr., suite 100
Woodbury, MN 55125
651-222-6050



3625 W 65th Street, suite 200
Edina, MN 55435
651-222-6050

DECLINE FOR RUBELLA VACCINE

I have been informed by Reproductive Medicine & Infertility Associates that I am not immune to Rubella (German Measles). This means I have not been exposed to Rubella or have not had the vaccine to develop a sufficient level of antibodies in my blood.

It has been recommended that I be vaccinated against Rubella prior to attempting pregnancy, in accordance with the American College of OB/GYN Guidelines. I have chosen, however, not to follow this recommendation.

If I become pregnant and acquire Rubella during that pregnancy I am at risk for the following congenital malformations (birth defects):

- 1) Eye lesions, including cataracts, glaucoma, microphthalmia, and various other abnormalities.
- 2) Heart disease, including patent ductus arteriosus, septal defects, and pulmonary stenosis.
- 3) Auditory defects.
- 4) Central nervous system defects, including meningoencephalitis.
- 5) Retarded fetal growth.
- 6) Hematologic changes, including thrombocytopenia and anemia.
- 7) Hepatosplenomegaly and jaundice.
- 8) Chronic diffuse interstitial pneumonitis.
- 9) Osseous changes.
- 10) Chromosomal abnormalities.

I have read and understand the above risks and decline to have the recommended rubella vaccine.

Patient Printed Name

ID #

Patient Signature

Date

Witness signature

Date



DECLINE FOR VARICELLA VACCINE

I have been informed by Reproductive Medicine & Infertility Associates that I am not immune to Varicella (Chicken Pox). This means I have not been exposed to Varicella or have not had the vaccine to develop a sufficient level of antibodies in my blood.

It has been recommended that I be vaccinated against Varicella prior to attempting pregnancy, in accordance with the American College of OB/GYN Guidelines. I have chosen, however, not to follow this recommendation.

If I become pregnant and acquire Varicella during that pregnancy in the first 20 weeks the baby is at risk for the following congenital malformations (birth defects) associated with congenital Varicella syndrome:

1. Scars on the skin
2. Muscle and bone defects
3. Malformed limbs
4. Vision problems
5. Mental retardation

I have read and understand the above risks and decline to have the recommended Varicella vaccine.

Patient Printed Name

ID #

Patient Signature

Date

Witness signature

Date



HYSTEROSALPINGOGRAM (HSG)

During an infertility evaluation, it is important to determine whether the uterus and fallopian tubes are normal. The hysterosalpingogram (HSG) is an effective and safe procedure employed by physicians in accomplishing this task. An HSG test allows for visualization of the inside of the uterus and fallopian tubes via x-ray, as described in the Patient's Fact Sheet provided by the American Society for Reproductive Medicine (ASRM) and in the HealthEast Radiology Care sheet entitled "Hysterosalpingogram."

As mentioned in the ASRM Fact Sheet, the most common serious complication of an HSG is a pelvic infection. The risk is low, but can be made even lower with the use of prophylactic antibiotics. Most authorities believe that the use of prophylactic antibiotics is only beneficial if a patient is at increased risk for an infection, or if the tubes appear to be abnormal at the time of the HSG. Thus RMIA only recommends their use in certain circumstances. Nonetheless every patient is provided with antibiotic prescriptions in case they are needed. One of these prescriptions is for doxycycline (for which another antibiotic is substituted if there is an allergy), and the other is for metronidazole.

Risk factors for an HSG-related infection include (1) a history of certain sexually transmitted diseases or pelvic infection; (2) a history of a tube that is blocked, diseased, or dilated (hydrosalpinx); (3) a history of tubal surgery; and/or (4) a history of a tubal pregnancy. It is RMIA's policy that all patients at increased risk start a 5-day course of doxycycline immediately before the HSG. Also, if doxycycline has not been started but the HSG reveals a blocked or diseased tube, the doxycycline is to be started immediately after the HSG. In this regard, you will use the reverse side of this form, to be completed by the radiologist or x-ray technician at the time of the HSG, to know whether or not you need to have the doxycycline prescription filled.

The metronidazole is only to be used when there is concern about a hydrosalpinx. It is RMIA's policy that patients known to have a hydrosalpinx start a 5-day course of metronidazole the morning of the HSG. Also, if the metronidazole has not been started but the HSG reveals a hydrosalpinx, the metronidazole is to be started immediately after the HSG. In this case again the use of the reverse side of this form will let you know whether or not you need to have the metronidazole prescription filled.

In addition to the use of antibiotics as described, we also recommend that you take two to four 200-mg Advil tablets (or generic equivalent) about 1 hour before the procedure so as to decrease any cramping which may occur during the test. Following the procedure, you may note some vaginal spotting and pelvic discomfort for 24 hours. If you should experience any abdominal cramping, fever, or heavy bleeding, please call RMIA for immediate assistance.

A less common problem is that of an allergic reaction to the iodine-containing contrast material instilled into the uterus during the HSG. Thus if you have a history of allergy to iodine, shellfish, or x-ray contrast material (discovered during an earlier procedure such as an intravenous pyelogram) please notify a RMIA nurse or doctor before the HSG is scheduled.

Finally, the timing of the HSG is important. In general it should be performed between days 5 through 10 of your cycle (after menstruation is over, but before ovulation). It is of vital importance that this test not be done if a pregnancy is present. Thus it is RMIA's policy to have a blood pregnancy test done, after your menses has started, to confirm that no pregnancy is present. This has to do with the fact that what may seem like a normal menstrual period can occur in the case of either a normal or abnormal pregnancy. Also, to assist in properly timing the scheduling of the procedure, oral contraceptives may be prescribed. To schedule the test, please contact our office on day 1 or 2 of your menstrual cycle, and please refrain from unprotected intercourse until after the HSG. A pregnancy test will be scheduled, and you will be informed of the result by a telephone call from a nurse.



TRANSVAGINAL PELVIC ULTRASOUND

When you begin ovulation induction, your ovarian response to treatment will be monitored by transvaginal pelvic ultrasound. This procedure is usually completely painless and performed by inserting a narrow ultrasound transducer into the vagina. The thickness of the uterine lining along with the number and size of the developing follicle(s) will be measured and recorded. The entire procedure usually lasts for a few minutes. It is important that you empty your bladder *before* you are called back for your exam.** **If you are wearing a tampon, it will need to be removed.**

A single ultrasound scan rarely provides enough important information. However, a series of these ultrasound scans in conjunction with other test results (i.e. blood hormone levels) will usually provide a precise assessment of follicular growth. Following the completion of the ultrasound, you will meet with a nurse to discuss your treatment plan.

**NOTE: If you are having a trial transfer or have been advised to have a full bladder for your procedure, please disregard the previous statement.



CLOMID CHALLENGE TEST

Your physician may recommend a Clomid Challenge Test (CCT) in order to assess your ovarian reserve. Ovarian reserve screening may provide a better estimate of how far you have progressed through your reproductive life than chronological age alone.

How the test works:

The test is based on the premise that in response to Clomid, patients with normal ovarian function will produce enough hormones to keep their FSH level within the normal range. If the FSH or estradiol level is elevated as a result of the Clomid, the prognosis for the patient achieving a pregnancy using their own oocytes is poor.

How the test is performed:

The test is performed by drawing blood in order to determine FSH and estradiol levels on day 3 of your cycle. In certain situations, a baseline ultrasound will also be performed on day 3.

You will be given a prescription for Clomid which is to be taken daily on days 5-9 of your cycle. Your FSH level as well as your progesterone level will be tested via blood draw on day 10 of your cycle.

Your physician will review your results with you.

- Cycle 1 = 1st day of period
- Cycle 2 = nothing
- Cycle 3 = FSH and E2 (lab appointment)
- Cycle 4 = nothing
- Cycle 5 = Clomid 100mg (2 tablets)
- Cycle 6 = Clomid 100mg (2 tablets)
- Cycle 7 = Clomid 100mg (2 tablets)
- Cycle 8 = Clomid 100mg (2 tablets)
- Cycle 9 = Clomid 100mg (2 tablets)
- Cycle 10 = FSH and Progesterone (lab appointment)



PATIENT'S FACT SHEET

Recurrent Pregnancy Loss

Recurrent pregnancy loss is a disease* distinct from infertility, defined by two or more failed pregnancies. When the cause is unknown, each pregnancy loss merits careful review to determine whether specific evaluation may be appropriate. After three or more losses, a thorough evaluation is warranted. Although approximately 25% of all recognized pregnancies result in miscarriage, less than 5% of women will experience two consecutive miscarriages, and only 1% experience three or more. Couples who experience recurrent pregnancy loss may benefit from a medical evaluation and psychological support.

Genetic/Chromosomal Causes. A chromosome analysis performed from the parents' blood identifies an inherited genetic cause in less than 5% of couples. Translocation (when part of one chromosome is attached to another chromosome) is the most common inherited chromosome abnormality. Although a parent who carries a translocation is frequently normal, their embryo may receive too much or too little genetic material. When this occurs, a miscarriage usually occurs. Couples with translocations or other specific chromosome defects may benefit from pre-implantation genetic diagnosis in conjunction with in vitro fertilization.

In contrast to the uncommon finding of an inherited genetic cause, many early miscarriages are due to the random (by chance) occurrence of a chromosomal abnormality in the embryo. In fact, 60% or more of early miscarriages may be caused by a random chromosomal abnormality, usually a missing or duplicated chromosome.

Age. The chance of a miscarriage increases as a woman ages. After age 40, more than one-third of all pregnancies end in miscarriage. Most of these embryos have an abnormal number of chromosomes.

Hormonal Abnormalities. Progesterone, a hormone produced by the ovary after ovulation, is necessary for a healthy pregnancy. There is controversy about whether low progesterone levels, often called luteal phase deficiency, may cause repeated miscarriages. Treatments may include ovulation induction, progesterone supplementation or injections of human chorionic gonadotropin (hCG), but there is no evidence to support the effectiveness of these treatments.

Metabolic Abnormalities. Poorly controlled diabetes increases the risk of miscarriage. Women with diabetes improve pregnancy outcomes if blood sugars are controlled before conception. Women who have insulin resistance, such as obese women and many who have polycystic ovarian syndrome (PCOS), also have higher rates of miscarriage. There is still not enough evidence to know if medications that improve insulin sensitivity lower miscarriage risks in women with PCOS (see Fact Sheet "Insulin Sensitizing Agents").

Uterine Abnormalities. Distortion of the uterine cavity may be found in approximately 10% to 15% of women with recurrent pregnancy losses. Diagnostic screening tests include hysterosalpingogram, sonohysterog-

raphy (See Fact Sheets "Hysterosalpingogram," and "Saline Infusion Sonohysterography"), ultrasound, or hysteroscopy. Congenital uterine abnormalities include a double uterus, uterine septum, and a uterus in which only one side has formed. Asherman's syndrome (scar tissue in the uterine cavity), uterine fibroids, and possibly uterine polyps are acquired abnormalities that may also cause recurrent miscarriages. Some of these conditions may be surgically corrected.

Antiphospholipid Syndrome. Blood tests for anticardiolipin antibodies and lupus anticoagulant may identify women with antiphospholipid syndrome, a cause for 3% to 15% of recurrent miscarriages. A second blood test performed at least 6 weeks later confirms the diagnosis. In women who have high levels of antiphospholipid antibodies, pregnancy outcomes are improved by the use of aspirin and heparin.

Thrombophilias. Inherited disorders that raise a woman's risk of serious blood clots (thrombosis) may also increase the risk of fetal death in the second half of pregnancy. However, there is no proven benefit for testing or treatment of women with thrombophilias and recurrent miscarriage in the first half of pregnancy.

Male factor. Increasing evidence suggests that abnormal integrity (intactness) of sperm DNA may affect embryo development and possibly increase miscarriage risk. However, these data are still very preliminary, and it is not known how often sperm defects contribute to recurrent miscarriage.

Unexplained. No explanation is found in 50% to 75% of couples with recurrent pregnancy losses.

Tests with no proven benefit for recurrent miscarriage include cultures for bacteria or viruses, tests for insulin resistance, antinuclear antibodies, antithyroid antibodies, maternal antipaternal antibodies, antibodies to infectious agents, and embryotoxic factors.

Treatments with no proven benefit include leukocyte (white blood cell) immunization and intravenous immunoglobulin (IVIG) therapy.

Conclusion. A couple may be comforted to know that the next pregnancy is successful in 60% to 70% of those with unexplained recurrent pregnancy losses. A healthy lifestyle and folic acid supplementation is recommended before attempting another pregnancy. Smoking cessation, reduced alcohol and caffeine consumption, moderate exercise, and weight control may all be of benefit. Counseling may provide comfort and help cope with the grief, anger, isolation, fear, and helplessness that many individuals experience after repeated miscarriages.

* Disease is "any deviation from or interruption of the normal structure or function of any part, organ, or system of the body as manifested by characteristic symptoms and signs; the etiology, pathology, and prognosis may be known or unknown." From: *Dorland's Illustrated Medical Dictionary*, 31st edition, 2007:535.

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NOTICE REGARDING SEXUALLY EXPLICIT MATERIALS

RMIA provides sexually explicit material to aid in the collection of sperm collection.

The materials which may be available at RMIA include: visual and audio depictions of nudity and explicit sexual situations. RMIA is not responsible for the content of the materials. Persons who may be offended by depictions of nudity and sexually explicit activities should not view these materials.

RMIA does not endorse these materials, but provides them as a service to our patients.



SEMEN ANALYSIS

Patient Information Sheet

A semen analysis is the most comprehensive test performed for male infertility. It consists of several different components: volume, pH, viscosity, appearance, motility, progression, concentration, white blood cells, supravital, agglutination, and morphology. Although some components have more clinical significance than others, the entire semen analysis will be reviewed by your physician in order to provide you with the most accurate clinical picture.

IMPORTANT NOTE: This laboratory procedure is billable through Infertility Laboratory and Surgery Center Associates (ILSCA) which does NOT participate with any insurance carriers. You will need to pay in advance before this procedure can be performed. The cost for a semen analysis is \$110.

1. All semen analyses appointments must be scheduled in advance by calling RMIA, Monday – Friday, 7:30am – 4:30pm.
2. Collection rooms available in:
 - Woodbury: Monday – Friday, 7:00am – 1:00pm.
 - Edina: Tuesday, Wednesday, Thursday, 7:00am – 1:00pm.
3. A two to seven day abstinence period from ejaculation is required on the day of your appointment. No other restrictions are necessary.
4. If you prefer to collect the specimen in the privacy of your home, obtain a collection kit from your provider or RMIA. The kit will include a sterile collection container, which has been pre-tested for toxicity to sperm, specimen collection instructions, off-site consent form, towelette, transport bag, and non-toxic lubricant upon request. Avoid commercial lubricants, oral stimulation, and intercourse during collection. Record on collection label if entire sample is not collected. The specimen should be delivered to the lab within 60 minutes after collection and kept next to the body during transit.
5. If problems occur and you are unable to provide a specimen, your appointment can be rescheduled. If you are on site, please inform the lab staff and they will assist you in rescheduling your appointment. If you are off site, please call the RMIA main number and the receptionist will reschedule your appointment.
6. Results of your semen analysis will be available in 5 working days. Laboratory staff is prohibited from providing and/or interpreting results. Please contact your physician's office.



SEMEN CRYOPRESERVATION

Patient Information Sheet

Semen cryopreservation is a procedure during which an ejaculate is frozen using a specialized media for possible use in treatment at a later date.

IMPORTANT NOTE: This laboratory procedure is billable through Infertility Laboratory and Surgery Center Associates (ILSCA) which does NOT participate with any insurance carriers. You will need to pay in advance before this procedure can be performed. The cost for the Semen Cryopreservation Procedure is \$400.

1. Infectious disease testing is a requirement when cryopreserving a semen sample.
2. All semen cryopreservation procedures must be scheduled in advance by calling RMIA, Monday through Friday, between 7:30 am and 4:30 pm.
3. Semen cryopreservation procedures are performed in the Reproductive Biology Laboratory, at the Woodbury clinic only; Monday through Friday from 7:00 am until 1:00 pm. Earlier collection times (7:00-9:00) may not be available for they are generally reserved for in-house procedures.
4. A two to seven day abstinence period from ejaculation is required on the day of your appointment. No other restrictions are necessary.
5. The preferred collection location is on site in the Reproductive Biology Laboratory. You will receive specific information regarding specimen collection at the time of your appointment.
6. If you choose to collect the specimen off site, you must obtain a collection kit from the Reproductive Biology Laboratory, during normal business hours (Monday through Friday, 7:00 am – 4:30 pm). The kit will include a sterile collection container, which has been pre-tested for toxicity to sperm, patient information sheet, specimen collection instructions, and transport bag. A cryo consent form, included in this kit, needs to be signed and the specimen must be delivered here within 60 minutes after collection.
7. If problems occur and you are unable to provide a specimen, your appointment can be rescheduled. If you are on site, please inform the lab staff and they will assist you in rescheduling your appointment. If you are off site, please call the RMIA main number and the receptionist will reschedule your appointment.
8. Results of your semen cryopreservation procedure will be available in 5 working days. Laboratory staff is prohibited from providing and/or interpreting results. Please contact your physician's office.



REPRODUCTIVE BIOLOGY LABORATORY INSTRUCTIONS FOR OFF-SITE SEMEN COLLECTION

All off-site collections require the use of a sterile container pre-tested for toxicity to sperm, which may be acquired from RMIA. The off-site collection kit contains:

- Instructions for off-site semen collection
 - Sample collection information form
 - Sterile semen collection cup
 - Antiseptic towelette
 - Off-site semen specimen collection
 - Biohazard bag
1. If not already labeled, label container with your first and last name and your RMIA clinic identification number. **UNLABELED CONTAINERS MUST BE DISCARDED!**
 2. Wash your hands with soap and water and then dry thoroughly.
 3. Cleanse head of penis with antiseptic towelette provided.
 4. It is extremely important that water, saliva, mineral oil, KY jelly, or any other form of commercial lubricant do not contaminate the sample, as these materials are toxic to sperm. The laboratory has non-toxic lubricant if needed.
 5. The specimen should be collected by masturbation only. Collect the entire ejaculate into the container, and be sure to secure the cover of the container tightly when you are done.
 6. Complete the enclosed forms with all requested information.
 7. Place the specimen in the biohazard bag provided and transport the specimen to the clinic. Keep the specimen at body temperature during transport! (i.e., placed in an inside shirt pocket). Any extremes in temperature may have a detrimental effect on specimen quality.
 8. The specimen should be delivered to the laboratory within 60 minutes of collection. Receiving the specimen beyond this time may have a negative impact on the quality of your test results.
 9. If you are unable to collect a specimen, your appointment may be rescheduled. Please call RMIA directly, and they will assist you in rescheduling.

For Optimal Results

A period of 2-7 days of abstinence (no ejaculation) should precede the collection of your specimen for semen analysis unless otherwise directed by your physician.





RETROGRADE EJACULATION

Patient Information Sheet

Retrograde ejaculation refers to the entry of semen into the bladder instead of going out through the urethra during ejaculation. Urine is usually spermicidal (kills sperm) because of its acidity and hyperosmolarity (greater concentration) relative to semen. If you have or are being evaluated for retrograde ejaculation the collection process will include urine and a semen specimen separately. The objective of the preparation portion is to increase the likelihood of dilute, alkaline urine in order to improve chances of sperm survival in the urine.

IMPORTANT NOTE: This laboratory procedure is billable through Infertility Laboratory and Surgery Center Associates (ILSCA) which does not participate with any insurance carriers. You will need to pay in advance before this procedure can be performed. The cost for this procedure is \$110.

1. All retrograde ejaculation evaluations must be scheduled in advance by calling RMIA, Monday through Friday, between 7:30 am and 4:30 pm.
2. Retrograde ejaculation evaluations are performed in the Reproductive Biology Laboratory, Monday through Friday from 7:00 am until 1:00pm. Earlier collection times (7:00-9:00) may not be available for they are generally reserved for in house procedures.
3. A 2-7 day abstinence period from ejaculation is required on the day of your appointment.
4. For 48 hours prior to semen collection increase daily fluid intake (at least 8 to 10- 8 ounce glasses, preferably water).
5. Void prior to collection.
6. Ejaculate semen into first cup for analysis
7. Void into separate cup(s) and save for analysis (Completely empty bladder and save all urine).
8. If you choose to collect the specimen off site, you must obtain a collection kit from the Reproductive Biology Laboratory. The kit will include a sterile collection container and several other containers, which have been pre tested for toxicity to sperm, patient information sheet, specimen collection instructions, and transport bag. The specimen must be delivered within 60 minutes after collection.
9. If problems occur and you are unable to provide a specimen, your appointment can be rescheduled. If you are on site, please inform the lab staff and they will assist you in rescheduling your appointment. If you are off site, please call the RMIA main number and the receptionist will reschedule your appointment.
10. Results of your retrograde ejaculation evaluation will be available in 5 working days. Laboratory staff is prohibited from providing and/or interpreting results.



CYSTIC FIBROSIS SCREENING

Cystic Fibrosis (CF) is one of the most common genetic diseases in the Caucasian population. Approximately 1 in every 25 Caucasians is a carrier for this recessive condition, and 1 in 2500 is clinically affected. CF can occur in any ethnic group, but the carrier frequency and disease incidence vary greatly. Cystic fibrosis has a broad clinical presentation ranging from congenital absence of the vas deferens to chronic lung disease, pancreatic insufficiency, ileus, failure to thrive, and infertility.

In 2001, the American College of Obstetricians and Gynecologists (ACOG) recommended that CF carrier screening be offered to all couples who are pregnant or are considering pregnancy.

CF Mutation Detection Rates for Various Populations

<u>Population</u>	<u>Mutation Detection Rate</u>	<u>CF Carrier Risk</u>
N. European Caucasian	90%	1/25
Ashkenazi Jewish	97%	1/29
Hispanic American	57%	1/46
African American	70%	1/65
Asian American	30%	1/90