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**REPRODUCTIVE GENETICS INSTITUTE**

**INFORMATION PACKET**

**IN VITRO FERTILIZATION (IVF)**

**WITH**

**PREIMPLANTATION GENETIC DIAGNOSIS (PGD)**

**FOR CHROMOSOMAL ANEUPLOIDY**

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## **INTRODUCTION TO PREIMPLANTATION GENETIC DIAGNOSIS (PGD)**

The Reproductive Genetics Institute (RGI) located in Chicago, Illinois performs the most advanced procedures for the identification of genetic disorders before birth. Couples considering PGD may already have a child with a genetic condition, may have terminated affected pregnancies following prenatal diagnosis, may carry a balanced translocation (placing their pregnancies at a high risk for miscarriage or abnormal outcome), may have had previous pregnancies that were chromosomally abnormal, or may be at increased risk for Down Syndrome and other chromosome abnormalities (due to advancing maternal age). RGI can assist you in your family planning by offering genetic counseling regarding PGD and In Vitro Fertilization (IVF) (which is associated with this advanced procedure.)

This packet will assist you in understanding PGD and IVF. Some parts of this packet may not apply to you, depending on your specific concerns and circumstances for considering PGD.

## **PREIMPLANTATION GENETIC DIAGNOSIS (PGD)**

The Reproductive Genetics Institute offers PGD to families at a high risk for producing offspring with genetic disorders. Performing genetic diagnosis prior to implantation may prevent the initiation of abnormal pregnancies and reduce the potential for the termination of affected fetuses diagnosed by prenatal testing.

For the past 19 years, more than 3500 unaffected babies have been born following IVF with PGD for chromosomal and single gene disorders. We offer PGD for chromosomal abnormalities, such as Down syndrome (trisomy 21), trisomy 18 or 13. We also perform PGD for chromosomal translocations and over 200 single gene disorders, such as cystic fibrosis, thalassemia, and Tay Sachs disease. It is possible to do PGD for almost all genetic disorders with an identifiable mutation.

PGD involves genetic testing of the oocytes and/or embryos obtained by undergoing In Vitro Fertilization (IVF). IVF is an assisted reproductive technology (ART) procedure in which fertilization of the egg occurs outside of the body in a controlled setting. The oocyte (egg) is removed from the woman's ovary and is placed with the male's sperm. If the sperm fertilizes the egg, the fertilized egg (zygote) begins to divide. Several techniques can be utilized in order to determine the genetic make-up of the embryo, depending on whether the diagnosis is for aneuploidies (extra/missing chromosomes), translocations, or single gene disorders. The genetic status of the embryo(s) can be determined before the embryo(s) is/are transferred into the uterus. This innovative technology is a valuable alternative available to couples who are at risk for a genetic condition. At this time, prenatal diagnosis by chorionic villus sampling (CVS) or amniocentesis is still recommended for reassurance and confirmation of PGD results.

The following procedures are thus necessary when undergoing PGD and IVF:

1. Ovulation Induction
2. Oocytes Aspiration
3. Fertilization and Embryo Culture
4. Polar body removal and/or blastomere biopsy
5. Genetic testing
6. Embryo transfer and implantation
7. Embryo Cryopreservation (if requested by patient)
8. Confirmation studies by CVS or amniocentesis (recommended but not required)

If you live outside of Illinois, it is possible for us to work with your local Reproductive Specialist for part (or all) of your cycle in an effort to reduce or eliminate the need for you to travel to Chicago.

## **Ovulation Induction**

Ovulation normally involves the release of a single mature egg from its follicle in the ovary. In the IVF process, multiple mature eggs are retrieved before they are ovulated. Medication is used during a woman's cycle in order to stimulate the eggs to mature simultaneously. The large majority of the medications used during an IVF cycle are administered by injection. Usually, there are three groups of medications used. The first group consists of medications that stimulate the ovary to produce more than one mature egg. These include Gonal F, Repronex, Follistim, and Pergonal.

In order to be able to collect the eggs, other medications are used to prevent spontaneous ovulation to occur. These medications include Lupron, Cetrotide and Antagon.

A third medication, human chorionic gonadotropin (hCG), is administered to trigger final oocyte maturation before the egg is retrieved. Progesterone may also be administered before egg retrieval to maintain a thick endometrial lining in order to promote implantation. Ovulation normally occurs 38 hours after hCG is administered; therefore, egg retrieval is timed 34-38 hours after the injection of hCG.

Ultrasound and blood tests carefully monitor the effects of the maturing follicles. The blood tests measure the amount of estradiol (E2) in the blood. Because follicles secrete E2, levels in the blood will show the follicles' responses to the medications. Vaginal ultrasounds show the number, location, and size of the follicles. The ultrasounds and blood tests will determine whether the follicles are ready to be retrieved. If the follicles are not well stimulated or the number of follicles is too small for the purpose of PGD, the cycle may be cancelled and a new cycle begun with different doses of medication.

## **Hyperstimulation Assessment:**

One of the risks of taking fertility medications is the possibility of ovarian hyperstimulation syndrome (OHSS). Severe OHSS may occur in less than 1% of cycles. Monitoring throughout the cycle can minimize the number of follicles and the level of estradiol produced by the follicles. If on the day that you are given hCG, your estradiol is between 3000-5000 pg/ml your eggs may need to be retrieved, fertilized, and the resulting embryos frozen, otherwise, there is a risk of complications due to hyperstimulation if you become pregnant this cycle. The embryos may be frozen and transferred in a different cycle. If the estradiol is more than 5000 pg/ml, prior to your egg retrieval, this cycle may even need to be cancelled (no egg retrieval), and medications adjusted the next cycle.

## **Oocytes Aspiration (egg retrieval)**

A small needle inserted in a guide attached to an ultrasonic probe is used to perform the aspiration of the follicle. Using ultrasound to guide the needle path, the physician directs the needle through the vaginal wall into the ovarian follicles. The needle is connected to a suction pump and the fluid from each accessible follicle within the ovary aspirated. The patient is usually awake but mildly sedated during this procedure by administering intravenous Demerol® or Versed® ("twilight sleep.") The patient can be put under general anesthesia for an additional cost.

The retrieved eggs are cultured for approximately 6 to 20 hours depending on maturity before being exposed to sperm.

## **Fertilization and Embryo Culture**

The laboratory testing procedures take place in a special laboratory in which all conditions are sterile. The egg cell prior to fertilization divides into two unequal cells. The larger cell is the mature egg that will be fertilized. The smaller cell (called a polar body) can be removed (polar body removal) and tested for its genetic composition (see below).

A semen sample is provided to the laboratory on the day of the egg retrieval. The sample is then processed in order to obtain an optimal sample for fertilization. When the sperm sample is normal and PGD is not planned, then regular in vitro insemination of the eggs is possible. Otherwise, a single sperm is injected into the egg by a procedure known as intracytoplasmic sperm injection or **ICSI**. At this time, a second polar body is released from the egg. The eggs will be fertilized using ICSI to maximize the rate of fertilization and to monitor the exact timing of polar body removal. Occasionally, fertilization does not occur, or occurs abnormally (which occurs to fertile couples as well).

After fertilization has taken place, the embryo is transferred to a special growth medium. The culture dishes are maintained in an incubator where the atmosphere, humidity, and temperature are carefully monitored and controlled.

## **Polar Body Removal**

As indicated above, the first polar body produced from the division of the egg can be removed and tested for its chromosome complement or to identify whether it contains the abnormal gene of concern. Upon penetration of the egg by the sperm (fertilization), but prior to the joining of the sperm's genetic material with the egg's genetic material, the egg undergoes another cell division, producing two unequally sized cells. The larger cell will join with the sperm's genetic material to create the pre-embryo, whereas the smaller cell is called the second polar body. Polar bodies have no known function. They are simply "by-products" of the egg's division. Once implantation occurs, the polar bodies disintegrate and are not part of the developing fetus. By testing the first and second polar bodies, the genetic make-up of the egg and maternal genetic contribution to the resultant embryo can be determined. Removal and genetic analysis of the polar bodies occurs on the first and second day after aspiration. One or more polar bodies may fail to provide a conclusive result. It is then necessary to confirm a diagnosis made on polar body analysis by performing blastomere biopsy. In these situations, it may be possible to perform blastomere biopsy (embryo biopsy) for further genetic analysis.

## **Embryo (Blastomere) Biopsy**

Blastomere biopsy (also known as embryo biopsy) involves the removal of one or two cells from the 4 to 8 cell pre-embryo (blastomere) for the purpose of preimplantation analysis. The egg will typically be fertilized by using intracytoplasmic sperm injection (ICSI). Following fertilization, the zygote begins to divide. On the third day following egg retrieval, the embryo is at the blastomere stage, and a cell may be carefully removed for genetic analysis. After removal of the cell(s) from the blastomere, the developing embryo is returned to the culture dish. Genetic analysis is performed separately on the removed cell(s).

At this early point of embryo development, all cells in the embryo are equivalent; thus, removal of a cell from the embryo at this stage does not remove anything critical for normal development. The embryo compensates for the removed cell and continues to divide.

The techniques related to PGD are not 100% accurate and RGI encourages all patients who have undergone PGD to have prenatal testing, as this is still the current standard of care.

### **Embryo Transfer and Implantation**

Once an embryo is predicted to be free from the genetic disease for which testing was performed, the embryo will be recommended for transfer. The patient and their IVF physician will determine the number of embryos that are transferred for one IVF cycle. The embryos may be transferred:

1. THREE DAYS after egg retrieval. This is possible if the genetic analysis is complete and conclusive by polar body analysis alone. OR
2. FIVE DAYS after egg retrieval, at the blastocyst stage. This is required for cases involving blastomere (embryo cell) biopsy.

Embryo transfer is typically a brief procedure accomplished by inserting a catheter (preloaded with embryos) into the uterine cavity. This procedure is often performed under ultrasound guidance and is generally no more uncomfortable than a pap smear. Although a quick procedure, it is necessary to remain at the IVF center in a reclined position for approximately 20-30 minutes after transfer. The embryos will initially be free floating and reclining should facilitate them implanting into the thick uterine lining. Traveling should be postponed for at least a day and restricted to being the passenger in a car.

Patients are routinely prescribed progesterone (injections cream, or suppositories) from the day they are given hCG until the day of their pregnancy test. The pregnancy test is performed ten to twelve days after the embryo transfer. It can be done at the center or at your doctor's office, but should be a blood test (not a home pregnancy test). If the pregnancy test is positive, your IVF physician will instruct you to continue taking progesterone for approximately 4-6 weeks, as this is important in maintaining a thick uterine lining.

### **Embryo Cryopreservation**

If extra embryos are available following egg retrieval, fertilization, genetic analysis, and transfer, patients will be counseled regarding the remaining embryos available for freezing. Patients will decide which embryos they wish to have frozen and transferred in future cycles. The cost for a frozen embryo cycle and transfer will vary depending on the patient and method of payment. However, the cost for a "frozen cycle" is typically significantly less than another IVF/PGD cycle.

## **Genetic Analysis Techniques**

### ***FISH - Fluorescent In-Situ Hybridization for Chromosomal Analysis***

The FISH procedure begins with cells either in metaphase or interphase (steps in active division) of the cell cycle. FISH utilizes highly specific DNA probes. These probes are made from pieces of recombinant DNA and bind to specific chromosome(s). A probe will attach (hybridize) to a specific DNA region on a particular chromosome, if that region is present. Once a probe binds with its targeted chromosome, the probe fluoresces or lights up. When multiple probes are used, each is labeled with a different fluorescent color. Under a fluorescent microscope the different chromosomes can be distinguished from one another, because each of these probes are identified by its unique fluorescent color.

Another critical component involved with the FISH procedure is a process called “fixation”. This refers to a laboratory technique by which the cells to be analyzed are “fixed” onto a slide, allowing the cells to become as flat as possible. Fixation is critical to thinning out the cellular membrane, which then allows the FISH probes to penetrate to the level of the DNA, and attach or hybridize to the chromosome.

FISH probes are available for many chromosomes. We use FISH probes when testing for chromosomal translocations and aneuploidies. It may be necessary to design a specific probe in the case of translocations, which enables us to “paint” the whole chromosomes that are involved with the translocation. In aneuploidy testing, we usually use FISH probes specific for 5-11 chromosomes. This allows us to determine if the correct numbers of these chromosomes are present in a cell. For example, if a patient has three copies of chromosome 21 in an embryo, the result would be Down syndrome. We offer different aneuploidy testing panels for up to 11 different chromosomes. Chromosomes 8, 9, 13, 15, 16, 17, 18, 21, 22, X and Y are included because abnormalities involving these chromosomes are responsible for 70-80% of failed implantation, miscarriage, and essentially all children born with numerical chromosomal abnormalities.

FISH probes can be used to determine of the sex chromosomes in the case of sex-linked disorders such as hemophilia, or in cases where there is an increased possibility of a sex chromosome disorder (e.g. if the male partner has severe male factor infertility). Other probes target specific regions or even specific genes of a particular chromosome and can be diagnostic of certain abnormalities.

## PROTOCOL FOR EVALUATION AND PARTICIPATION IN PROGRAM

1. After reviewing this information packet, please contact one of our genetic counselors/PGD coordinators for information regarding our center's services by calling (773) 472-4900 or email them at rgiworld@gmail.com. They will be able to answer questions regarding our center and what test results or paperwork is required. They will also be able to give you information regarding the costs for PGD and/or IVF.
2. If you are located in the Chicago area and want to do both the PGD and the IVF in one place, our genetic counselors will place you in contact with our Reproductive Specialist.
3. After talking with a genetic counselor, you will be sent the necessary paperwork required for PGD. A PGD consent form and Requisition form along with payment are necessary prior to your egg retrieval.
4. You have the option of undergoing IVF at our IVF center OR at another center local to you. If your chosen IVF center cannot perform the required biopsies for your case, we may be able to send one of our experienced embryologists to your center to perform the biopsies for your case\*.

\*If you chose to pursue IVF outside of RGI, and need an RGI embryologist to travel to your center for the biopsies it is important that ensure that your local IVF center has the appropriate equipment required by our staff. If your local IVF center does not have our required equipment and/or biopsy experience, you may prefer to come to RGI for your IVF cycle OR transport your embryos (in a portable incubator) to our center for the biopsy and testing.

If you would like to pursue **your IVF cycle at RGI in Chicago**, the steps are as follows:

- a) Please call our IVF department at 773-472-4949 to arrange a new patient consultation with our Reproductive Specialist, Dr Ilan Tur-Kaspa. This consult can be done over the phone or in person. There is a non-refundable fee for this consultation.
- b) Please complete the following lab checklist (pages 11-12, **Patient lab work-up before either IVF alone or IVF-PGD\***). These tests must be performed in the past 6-12 months, and can be arranged through our office or your local OBGYN or IVF center.
- c) Our Reproductive Specialist will be responsible for reviewing all test results and for choosing the medication protocol for ovarian stimulation.
- d) You must have a center to monitor you while on IVF medications. This monitoring can be done through our office or through a center closer to your home. The monitoring results (blood test and ultrasound results) must be sent to our IVF center for review. Our IVF Coordinator will request from you the contact information for the monitoring center; so that we may be keeping abreast as to your cycle's progress.
- e) You may arrive in Chicago before or during ovarian stimulation and complete the monitoring here, or you may wait and arrive one day before the Egg Retrieval. We need you and your male partner (or his frozen sperm sample) to be in Chicago on the day of

egg retrieval. You may expect embryo transfer (ET) to be performed 5 days after the egg retrieval. You may plan your return trip the following day.

If you would prefer to **pursue your IVF cycle in a center in your area**, this may be possible. If this is the desired option:

- a) Contact one of our genetic counselors to determine whether there is a center in your area with which we have already established a working relationship. If so, we may refer you to this center for your IVF cycle.
- b) If there are no centers in your area with which we have a working relationship, we will assist you in locating such a center and contacting them regarding their willingness to establish a relationship with RGI for the purposes of offering PGD.
- c) Once a site is selected, this information should be shared with your RGI genetic counselor, including contact information. She will send you a requisition form and consent form for the PGD. The consent form needs to be signed, notarized and returned (original copy, please, no faxed copies) along with the payment for the PGD. **This payment and the consent must be received prior to starting medications.**
- d) If your entire IVF cycle will be completed in your area and you are working with an IVF center that is experienced in performing its own biopsies, an RGI embryologist will NOT be involved. **You will only need to make payment for the PGD.**
- e) If your entire IVF cycle will be completed in your area and you are working with an IVF center that **cannot** perform their own biopsies, your case will require one of our embryologists to travel to your area to perform the removal of the polar bodies and/or /blastomere for the purpose of the PGD. **The PGD costs as well as the costs associated with the travel of this individual and the biopsy fee will be incurred by you, and you will be responsible for paying these fees prior to starting medications.**
- f) You should contact our genetic counselors when you have a written protocol of how your cycle is expected to be conducted (many centers use a “calendar” format). Specifically, we must know the date Lupron is begun and when stimulation is started. Additionally, we will need updates, either from yourself or the nurse coordinator in charge of your case, on how your IVF cycle is progressing. **Finally, it is critical to make contact with our center once you have been instructed on when to administer the hCG shot (or trigger shot) so that travel plans can be finalized and our lab can be ready for your case.**

## **PAYMENTS**

- a) Regarding insurance coverage: Please contact your insurance company regarding the coverage for IVF medications, IVF treatment, PGD biopsy procedures and/or PGD. If your medical insurance does cover one or more of the above, we require that all payment be made in full prior to beginning a cycle. Therefore, it is your responsibility to pay these costs up front. RGI is willing to submit claims to your insurance company and reimburse you any money owed to you.

- b) You are responsible for all fertility medication costs. You should check with your insurance regarding possible coverage of these medications. A prescription will be provided to you by you Reproductive Specialist for all needed medications and it can be arranged that they all will be shipped to you.
- c) Payment for your IVF/PGD cycle in is due once you are on stimulation prior to your egg retrieval. Additionally, all consents for the IVF and/or PGD cycle need to be signed and returned to us (original copies, no faxed copies, please) at the time of payment. Your PGD coordinator will provide you with the appropriate consent forms. We accept Visa, MasterCard, American Express, personal check or wire transfer.

**\*Initial Fertility Work-Up:** This should be completed with your local physician or fertility specialist (the cost of this work-up is not included in the cost for IVF at our center and will vary from center to center). If necessary, these tests may also be performed by our Reproductive Specialist. The following page contains the tests required prior to your initial consultation. Feel free to use this page to record your test results; however, the original laboratory reports will be required by our Reproductive Specialist.

\* This work-up is required only if coming to Chicago for your IVF cycle.

If egg retrieval and embryo transfer will be performed in another location (and only the PGD testing will be done at RGI) then all fertility and medical work-up and treatment will be performed by your Reproductive Specialist according to his or her protocols.

**INSTITUTE FOR HUMAN REPRODUCTION / REPRODUCTIVE GENETICS INSTITUTE**  
**PATIENT LAB WORK-UP BEFORE IVF or IVF-PGD**

Female Patient Information

Date: \_\_\_\_\_

Name (Last, First, Middle):			Date of Birth:		
Address:					
City:		State:	Zip:	Country:	
Tel: (H)		(Cell)	(W)	SSN/ID #:	

Test	Test Date	Test Results			
CBC		Hb:	HCT:	PLT:	WBC:
Fasting Glucose					
Blood Type and Rh					
Rubella Ab					
Varicella Ab (If applicable)					
CMV Ab		IgG:	IgM:		
TSH					
RPR (VDRL)					
Hepatitis B Surface Ag					
Hepatitis C Ab					
HIV Antibody					
Day 3 FSH					
Day 3 LH					
Day 3 E2					
Day 3 Prolactin					
Cervical Cultures		Gonorrhea:		Chlamydia:	
PAP Smear (w/in one year)					
Uterine Cavity Assessment		(HSG, Hysterosonogram, or Hysteroscopy)			
		Normal cavity / _____			
Day 2-3 Ultrasound		<b>Antral Follicles count:</b> # RT: _____ # LT: _____ Uterus: AV / RV Size: _____ Fibroids: No / Yes _____			
<b>Physical examination</b>		W.N.L / _____			
<b>Mammogram (age &gt; 40 Y)</b>					
<b>Medical clearance (if needed)</b>					

Genetic carrier screen (as applicable)					
Test	Test Date	Results	Test	Test Date	Results
Cystic Fibrosis			Karyotype		
Tay-Sachs					
Canavan					
Familial Dysautonomia					
Hemoglobin electrophoresis					

Form completed by IVF Coordinator: NT / MF and patient is ready to start cycle.

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

**INSTITUTE FOR HUMAN REPRODUCTION / REPRODUCTIVE GENETICS INSTITUTE**  
**PATIENT LAB WORK-UP BEFORE IVF or IVF-PGD**

Male Partner of \_\_\_\_\_ Date: \_\_\_\_\_

Name (Last, First, Middle):	Date of Birth:
SSN/ID #:	
Tel: (Home)	(Cell) (Work)

Semen Analysis	Test Date	Test Result
Volume:		
Concentration:		
% Motility:		
% Normal Sperm (by Kruger or WHO Criteria)		

Test	Test Date	Test Results
RPR (VDRL)		
Hepatitis B Surface Ag		
Hepatitis C Ab		
HIV Antibody		

Genetic carrier screen (as applicable)					
Test	Test Date	Results	Test	Test Date	Results
Cystic Fibrosis			Karyotype		
Tay-Sachs					
Canavan					
Hemoglobin electrophoresis			Familial Dysautonomia		

- **Strongly Recommended Genetic Carrier Screening for the couple (as needed):**
  - **All PATIENTS** (Caucasians/Hispanics/African American) –**Cystic fibrosis**.
  - **Patients of Jewish Origin** – Recommending Tay Sachs; Canavan; and Familial Dysautonomia; and also Gaucher, Bloom; Niemann-Pick; Fanconi’s Anemia; Mucopolidosis Type IV.
  - **Patients of French Canadian and Cajun Origin** –Tay Sachs (enzymatic).
  - **Patients of Mediterranean** (Greek or Italian) and of Southeast Asian Origin–Hemoglobin electrophoresis for Thalassemia.
  - **Patients of African or African American Origin or Caribbean Hispanic Origin**–Hemoglobin electrophoresis for Sickle cell disease.
  - **Patients with Family history of Mental Retardation**–Fragile X.

**Dear Patient / Referring Physician:**

Certain tests must be performed prior to IVF treatment. Some are required by law and others by national standards of care. All tests are important to rule out problems that could reduce your chance of conception or increase the risk to mother or baby. Thank you for your cooperation.

Ilan Tur-Kaspa, MD

Form completed by IVF Coordinator: NT / MF and patient is ready to start cycle.

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

**We have provided the following information as an example of what is involved with one IVF cycle. The timing of IVF cycles and the medications taken during an IVF cycle will vary from patient to patient. Your Reproductive Specialist will prescribe your IVF medications.**

Prior to starting your IVF cycle, it is common for your physician to put you on birth control pills for few weeks in order to regulate your menstrual cycle.

The first day that you begin your menstrual cycle is commonly referred to as Day 1. Twenty-one days after Day 1, you will start taking a medication called Lupron. Within 10-14 days after being on Lupron, you will get your period. You will then have a baseline ultrasound examination and will start taking stimulation medications within a few days.

Stimulation involves lowering your dose of Lupron and starting to take stimulation medications (ie. Gonal-F, Repronex, Follistim, Pergonal). These medications will be taken for approximately 9-12 days.

If Lupron will not be used, but Cetrotide or Antagon, then you will start the stimulation medication first (on day 2 or 3 of cycle) and only after 5-7 days this newer medication will be added.

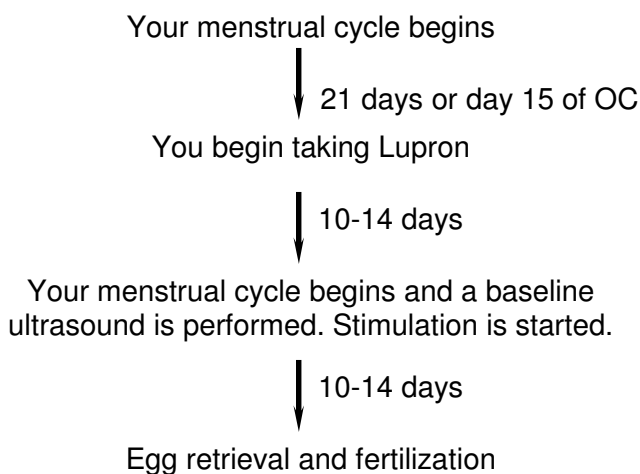
While you are undergoing stimulation, you will be monitored by blood tests and ultrasounds. During the ultrasounds, the number and size of follicles will be monitored.

When some of the follicles reach a size of 18-20 mm, you will be administered hCG (human chorionic gonadotropin). You will stop taking Lupron and the stimulation medications.

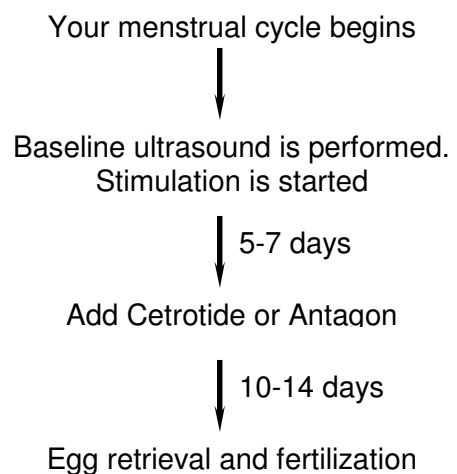
Approximately 35 hours after hCG is administered, the eggs will be retrieved. Three to five days after egg retrieval, embryo transfer will occur.

\* Your IVF cycle may vary depending on your age and response to the IVF medications.

### IVF CYCLE EXAMPLE 1



### IVF CYCLE EXAMPLE 2



## **Confirmation studies of genetic testing**

We recommend that all patients undergo prenatal diagnosis (CVS, amniocentesis) following preimplantation genetic diagnosis for the purpose of reassurance and confirmation. We will be happy to confirm aneuploidy testing in our clinical cytogenetics laboratory. Our genetic counselors can help you coordinate this testing, if needed.

The two common methods of diagnostic prenatal testing —chorionic villus sampling (CVS) and amniocentesis, are briefly described below. Our genetic counselors are available to discuss prenatal diagnosis options, if you have further questions or concerns.

### ***Chorionic Villus Sampling(CVS)***

CVS is typically performed between 10 and 12 weeks of pregnancy (first trimester). This can be beneficial to couples who wish to have prenatal test results earlier in the pregnancy. This allows for the option of a first trimester termination in the event of an abnormal result.

CVS involves the withdrawal of placental tissue (chorionic villi) under continuous ultrasound monitoring either transcervically or transabdominally. The placental tissue or villi is derived from the same cells as the baby. Therefore, by testing the chromosomes in the villi, we are indirectly testing the baby's chromosomes. These cells are analyzed for chromosomal abnormalities, such as Down syndrome. RGI performs both direct and tissue culture analysis to assure greater accuracy and for the provision of preliminary results in 5 days. CVS does not provide information on neural tube defects. If a patient chooses to have a CVS, a Maternal Serum Alpha-Fetoprotein screen (blood test) and/or fetal ultrasound at 15 to 18 weeks is recommended to detect neural tube defects.

### ***Amniocentesis***

Amniocentesis is typically performed between 15 and 20 weeks of pregnancy. This procedure involves the removal of a small amount (one ounce) of amniotic fluid from the amniotic sac (where the fetus is located) under continuous ultrasound monitoring. Within the amniotic fluid are fetal skin and amniotic cells, which can be analyzed for chromosome abnormalities, such as Down syndrome. To identify the presence of neural tube defects, such as anencephaly and spina bifida, the level of alpha-fetoprotein (AFP) in the amniotic fluid is also measured. An elevated level of AFP may indicate the presence of a neural tube defect. If there is an elevated level of AFP, another test called an acetylcholinesterase (AChE) assay is performed. AChE in the amniotic fluid confirms the presence of an open neural defect. AChE detects 99% of open neural tube defects.

Fetal ultrasound is also recommended.

For chromosomal analysis, result-reporting times are typically within 5 days for CVS results and 7-10 days for amniocentesis results. At RGI, we have been performing CVS and amniocentesis on a clinical basis for over 25 years.

## MEDICAL TERMINOLOGY

**Assisted Embryo Hatching** – a procedure in which a hole is made in the zona pellucida of the early embryo. The embryo may more easily “hatch” out of the zona through the hole around the time of implantation.

**Assisted Reproductive Technologies (ART)** – a collective term which refers to a variety of medical procedures used to achieve pregnancy.

**Aneuploidy** – An abnormal number of chromosomes. An extra chromosome is called a Trisomy and a missing chromosome is called a Monosomy.

**Blastocyst** – the stage of development that the embryo is in when it enters the uterine cavity for implantation (typically 5-6 days after fertilization)

**Blastomere** – a single cell from the developing embryo

**Chemical Pregnancy** – A positive hCG level in the blood that fails to continue to rise and does not lead to a clinical pregnancy.

**Clinical Pregnancy** – When a positive hCG level is obtained and a fetal sac is seen in the uterus during an ultrasound.

**Controlled Ovarian Hyperstimulation (COH)** – The use of medications to stimulate growth and development of multiple ovarian follicles.

**Cryopreservation** – Freezing and storage of excess embryos from an ART procedure in liquid nitrogen tanks. May be thawed and transferred at a later date.

**Embryo Transfer** – A procedure during which embryos are placed into the uterus. This can occur on day 3 (around the 4-8 cell stage) or day 5 (blastocyst).

**Estradiol (E2)** – A steroid hormone produced by the growing ovarian follicle that is measured to assess the response of the ovaries to stimulatory medications.

**Follicle** – A structure in the ovary that has nurtured the ripening egg and from which the egg is released or retrieved.

**Follicle Stimulating Hormone (FSH)** – A hormone produced by the pituitary gland that stimulates the ovary to ripen a follicle for ovulation.

**Follistim** - Acts directly on the ovary to stimulate development of follicles (eggs)

**Intracytoplasmic Sperm Injection (ICSI)** – An assisted fertilization technique in which a sperm is microinjected directly into the egg cytoplasm.

**In Vitro Fertilization (IVF)** – A procedure during which an egg is removed from a ripe follicle and fertilized by a sperm outside the human body.

**Genetic counselor** – a medical professional with specialized training in clinical genetics

**Gonadotropin Releasing Hormone (GnRH)** – A hormone produced by the hypothalamus that stimulates release of FSH and LH from the pituitary gland.

**GONAL-F** - Acts directly on the ovary to stimulate development of follicles (eggs)

**Human Chorionic Gonadotropin (hCG)** – A hormone secreted by the trophoblast that prolongs the life of the corpus luteum beyond its usual fourteen-day life span, resulting in the production of sufficient progesterone to support a pregnancy. It may be injected following controlled ovarian hyperstimulation to trigger ovulation and ensure adequate corpus luteum function. This hormone is the basis of most pregnancy tests.

**Lupron** – Synthetic gonadotropin releasing hormone analog administered to suppress secretion of LH and FSH to prevent premature ovulation.

**Luteinizing Hormone** - A hormone produced by the pituitary gland that triggers ovulation.

**Meiosis** – this term describes cell division that occurs during the formation of the mature egg and sperm. During meiosis, the number of chromosomes (genes) is reduced so that the egg and sperm contribute only half of the parent's genes to the embryo.

**Nondisjunction** – The failure of a chromosome pair to separate correctly during meiosis (cell division).

**Ovulation** – The release of an egg from the ovary

**Pergonal** – Acts directly on the ovary to stimulate development of follicles.

**Polar body** – a polar body is a small cell that is naturally released by the egg or oocyte during the process of meiosis. The first polar body is released by the oocyte at the time of ovulation. The second polar body is released by the oocyte, at the time of fertilization. The polar bodies do not contribute to the developing embryo, but are naturally discarded by the oocyte during the process of meiosis.

**Progesterone** – Given to raise progesterone levels to promote preparation of the endometrium for implantation of an embryo.

**Repronex** – Acts directly on the ovary to stimulate development of follicles.

**Translocation** – A chromosomal rearrangement in which chromosome segments are exchanged between chromosomes.

## FREQUENTLY ASKED QUESTIONS

**Q:** What is my first step?

**A:** Contact one of our genetic counselors to get information regarding the process, cost and to setup a free consultation. You can reach us by phone (773) 472-4900 or by email at [rgiworld@gmail.com](mailto:rgiworld@gmail.com).

**Q:** How many embryos do they put back?

**A:** This depends upon when they are put back—on day 3, they generally transfer up to three embryos. On day 5, they usually will not transfer more than two embryos. This is decided by the couple and the physician based on how many there are, their quality, and personal issues.

**Q:** How many eggs are typically retrieved?

**A:** This depends upon a number of variables—the younger the woman, the more eggs it is likely to get. There's no way to predict how many eggs will be retrieved, but we like to see at least 6 good follicles or we're likely to cancel the cycle.

**Q:** What happens if my cycle gets cancelled?

**A:** The physician will prescribe a different protocol than the previous one. This can be different medications, different dosages, put a woman on birth control pills, etc. It will be different for each couple. If your cycle is cancelled, we will refund your money (if you so desire) or can keep it for the next cycle. Depending upon when the cycle is cancelled, a portion of the monies may be kept to cover our costs.

**Q:** What percentage of embryos will be abnormal after aneuploidy testing?

**A:** This depends upon a number of variables—the younger the woman, the fewer chromosome problems we will find. The older the woman, the higher percentage of abnormal embryos we will find. Other factors like pregnancy and infertility history may also lead to a higher percentage of abnormal embryos than expected due to age.

**Q:** Do I have to travel to Chicago to pursue PGD with RGI?

**A:** For couples who would like both the IVF and PGD to be performed all in one place, it is necessary for you to travel to Chicago for the egg retrieval, testing and transfer. For those couples who would like to do IVF elsewhere and PGD with us, they will NOT need to travel to Chicago for any portion of the process.

**Q:** How long has RGI been doing PGD?

**A:** RGI has been performing PGD since it became available in 1990. We pioneered the polar body removal technology and are one of the most active centers offering PGD in the world. Our lab technicians are well trained in all techniques involved.

**Q:** What is the pregnancy rate?

**A:** There is no difference in pregnancy rates for couples going through IVF and PGD vs. couples going through just IVF. This is very age dependent, but as a general rule, it is ~30-40% per IVF cycle.

**Q:** Can you perform Aneuploidy testing on blastocysts?

**A:** Yes, blastocyst (trophectoderm) biopsy can be performed on blastocysts and aneuploidy testing can be done. Due to the timing it is recommended that the biopsy, testing and transfer all be done at RGI but it is possible to do it in conjunction with a cycle through an outside IVF center as well.

**Q:** Will my insurance cover this procedure?

**A:** In some instances, insurance companies have been found to cover the PGD testing and/or biopsy procedures. Some insurance companies will cover the IVF procedures (although usually this requires a diagnosis of infertility). You should contact your insurance directly to see if they will cover any or all of the procedures.

**Q:** Is there a waiting list?

**A:** No, there is no waiting list. Please contact a genetic counselor directly to get the process started.

**Q:** What if I'm on the birth control pill now, should I stop this?

**A:** It depends upon the type of birth control pill. It will be important to check with your IVF physician before making any changes to your pill.

**Q:** What is the risk for multiple births (e.g., twins or triplets)?

**A:** This will depend upon the number of embryos transferred and the quality of the embryos transferred. Most centers see a ~5-10% rate of multiple gestation.

**Q:** Where can I find more reading material regarding PGD?

**A:** Your genetic counselor can provide you with a list of relevant publications.