IVF Patient Information Packet

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Overview of Packet:

1. **Basic Timeline for IVF**.
2. **Preliminary Testing**.
3. **Medications to produce multiple eggs.**
4. **Procedures- what to expect.**
5. **Sample Protocol Calendars.**

1. Basic Timeline for IVF.

Generally some preparation and testing is required in order to optimize IVF treatment. It is realistic to assume that you will need about 2 months to cover the topics below.

Month 1. Testing Begin Lupron(if on long protocol)	Month 2. Stimulation, egg retrieval, embryo transfer

2. Preliminary Testing.

Month 1. (1st day of bleeding is considered cycle day (CD) #1)

A. CD#3 –FSH level (Follicle Stimulating Hormone), Estradiol

This is an assessment of ovarian reserve. The clomid challenge test may be used in a prior month. Please refer to the handout 'Ovarian reserve and Infertility'. If a patient has an elevation of FSH we may change the stimulation protocol. If the FSH is over 20 mIU/ml the outcomes for IVF are very poor and we need to discuss options. An FSH between 15mIU/ml and 20 mIU/ml may be considered the 'grey zone'. An FSH below 12 mIU/ml is associated with normal ovarian reserve. We now have some therapies that may improve ovarian function and have had pregnancies in patients with higher FSH levels.

B. Routine Blood Testing

All couples are tested for Hepatitis B, HIV I and II, and Hepatitis C.

C. Hormonal Evaluation

Patients with Polycystic Ovarian Syndrome (PCOS) will benefit from the additions of insulin sensitizing drugs to the stimulation protocol. We want to completely evaluate any hormonal condition that may affect the outcome.

D. Hysterosalpingogram (HSG) or Saline Infusion Sonogram (SIS).

It is important to have an assessment of the fallopian tubes before IVF. If a patient has dilated tubes (hydrosalpinges) studies have shown that the pregnancy rates with IVF are decreased. It is possible that fluid in the fallopian tube goes back into the uterine cavity and decreases implantation. Studies show that excision of the dilated tube improves pregnancy rates. This X-Ray study is done in the hospital Radiology Department by Dr. Donahue. It is acceptable if this procedure was performed in the initial infertility work-up. The Saline Infusion Sonogram evaluates the uterine cavity and uterine wall simultaneously. A small catheter is placed in the uterine cavity while we do a transvaginal ultrasound exam. We slowly inject saline which will fill the uterine cavity, exposing any polyps, sub-mucosal fibroids or scar tissue that could affect implantation. Additionally, at the time of the SIS we will do a **TRIAL EMBRYO TRANSFER** using a catheter similar to the actual transfer catheter. Studies have shown that the embryo transfer is the most important technical part of the IVF procedure. The correct placement of the embryos is essential and prior knowledge of the anatomy of the cervical canal crucial. Dr. Donahue does all of the embryo transfers. The trial embryo transfer is an appointment that is scheduled with Dr. Donahue and is completed in the office (North or South office).

E. Semen Analysis.

This should be done on all partners and be within a few months of the procedure. If a low sperm count is confirmed and ICSI (Intracytoplasmic Sperm Injection) planned, several tests including chromosome analysis and Cystic Fibrosis testing may be ordered. Our web site reviews many issues related to male factor infertility. Also, this test must be **scheduled** with our embryologist. Please call our office first to schedule an appointment as this can only be done on certain days of the week depending on our IVF schedule. We will cryopreserve a sample of the sperm incase the sample is poor on the day of egg retrieval or there is a problem with collection or the partner is out of town or ill.

F. Other

Neither partner should smoke, take herbal or other supplements/medications unless prescribed or OK'd by Dr. Donahue. Always check with us before any significant changes in diet, lifestyle, or activity.

3. Medications to produce multiple eggs.

The medications you will take in preparation for the egg retrieval are referred to as the drug "protocol". Each patient's protocol is unique, and determined by Dr. Donahue based on previous medical history. There is an "ART" to ovarian stimulation and we sometimes cancel a cycle is the stimulation is inadequate rather than have poor egg quality and a poor outcome. We have several different protocols. Possible medications include:

A. ***LUPRON*** (Luprolide acetate- 2-week kit)- *Lupron* acts upon the pituitary gland in the brain to alter the secretion of FSH and LH (the two hormones responsible for egg development and ovulation). Initially, *Lupron* will cause increased secretion of the two hormones, with a subsequent rise in estrogen secretion. Continual administration of *Lupron*, however, will lead to a suppression of the pituitary hormones, with subsequent drop in estrogen production. When we perform the baseline ultrasound exam on day 1 - 3 of the cycle we assess the degree of suppression by measuring the LH and estradiol levels. Occasionally we cancel a cycle if the estradiol level remains elevated for an

extended period. In ART stimulations, *Lupron* will allow the ovaries to produce more eggs without the fear of premature ovulation. ***Microdose Lupron*** is a low dose preparation that has the ability to stimulate rather than suppress the ovaries. This is used for 'poor responders' and some patients that do not do well on the basic 'Long *Lupron* Protocol.'

Administration: *Lupron* is taken as a subcutaneous injection, once per day, beginning on or about cycle day 21 in the month prior to egg retrieval.

Side effects: headaches, fatigue, mood-swings, hot flashes, delayed onset of your period, bruising or irritation at the injection sites

B. GONADOTROPINS (*Menopur, Repronex, Gonal-F, Follistim, Bravelle*) These drugs will act upon the ovaries, to cause the oocytes (eggs) to develop and grow. Usually, several oocytes develop on each ovary. They contain either pure FSH or FSH and LH.

	FSH	LH
Menopur, Repronex	75 IU	75 IU
Gonal-F, Follistim	75 IU	---
Bravelle	75 IU(97%)	3%

Administration: Gonadotropins must be administered by intramuscular injection or subcutaneously once or twice per day, according to your particular protocol. They are started when baseline tests (ultrasound and blood tests) indicate that the ovaries are in a resting, non-productive state.

Side effects: mood-swings, discomfort around the ovaries, abdominal fullness, soreness at the injection sites.

C. HCG (human chorionic gonadotropin; *Profasi, Pregnyl, Novarel*)- This hormone is taken once testing indicates the oocytes on the ovaries are ready to be released. It performs two functions: structural changes inside the eggs to make them able to be fertilized and expansion of the fluid inside the follicles (egg sacs) that would eventually lead to rupture and ovulation. Ovulation normally occurs between 36-42 hrs. after HCG administration.

Administration: HCG must be taken as an intramuscular injection. You will be given a specific time to take this injection- approximately 36 hours before your scheduled time for egg retrieval. The powder is mixed with **2cc's ONLY** of saline prior to injection.

Side effects: discomfort around the ovaries, soreness at the injection site.

D. ANTIBIOTIC (Doxycycline, Tetracycline, *Keflex*) Generally, only the female partner will take antibiotics. When performing the procedure to retrieve the eggs, a needle is placed through the vaginal wall and into the abdominal space. We want to minimize the risk of an infection due to this puncture, as fevers are not good for

developing embryos. If the male partner has white blood cells present in semen analysis sample, he will be treated with antibiotics also.
Administration: Doxycycline/Tetracycline: 1 tablet twice per day, by mouth, with meals, from the day of HCG administration until egg retrieval or: *Keflex*: 1 tablet three times a day for 7 days.
Side effects: stomach upset, allergic reactions (hives, itching, swelling) vaginal yeast infections in women.

E. PROGESTERONE

This hormone will act upon the lining of the uterus (the endometrium) to make it receptive for embryo implantation. As part of the egg retrieval process, progesterone-producing cells are removed along with the follicular fluid and oocytes, making the ovaries unable to produce progesterone sufficiently. Progesterone is vital for endometrial development and continued embryo support. It is absorbed by the body most efficiently through intramuscular injections. Also, intra-vaginal progesterone has been shown to decrease uterine contractions before embryo transfer and improve pregnancy rates. Please see the attached IVF protocol.
Administration: Intramuscular injections of 2cc's daily are begun one day after retrieval and continue (daily) through 10 – 12 weeks of pregnancy.
Side effects: breast tenderness, soreness at the injection sites, delayed onset of your period (even in the absence of pregnancy)

F. PRE-NATAL VITAMINS

Studies have shown that increasing the intake of folic acid prior to conception helps to decrease the chances of certain spinal-cord-defects in babies. It is also a good idea from a general health point of view to be on these multi-vitamins, prior to and throughout pregnancy.
Administration: 1 tablet per day, usually at bedtime
Side effects: stomach upset, nausea, constipation

G. METHYLPREDNISOLONE (*Medrol*)- This steroid hormone is taken when the Assisted-Hatch procedure is being done, in conjunction with the Embryo Transfer. It is taken to suppress any inflammatory reaction that might occur between the embryo(s) and the endometrial lining.
Administration: 1 (16mg) tablet, by mouth, once per day, OR 4 (4mg) tablets, by mouth, once per day.
Side effects: fluid retention

H. LOW-DOSE ASPIRIN- (Children's aspirin/baby aspirin) A very high blood level of estrogen, which will result from the gonadotropin drugs, can have the potential effect of increasing the coagulation factors in the bloodstream (especially in the small vessels that supply the uterus and ovaries). Aspirin, in low doses, will decrease the effects of those clotting factors, and in turn, increase blood flow to the tissue.

Administration: 1 (81mg) tablet, by mouth, per day.

Side effects: stomach upset, prolonged bleeding time

I. DEXAMETHASONE (*Decadron*)- Patients who are found to have an immunologic problem (presence of certain antibodies) that could be potentially affecting their fertility will be given a course of this steroid medication. Steroids work by suppressing the body's response to detected antibodies.

Administration: 1 (0.5mg) tablet daily, at bedtime.

Side effects: Reported side-effects normally occur only at higher doses, and when taken for extended periods of time.

J. ESTROGEN PILLS *(Estrace)*

Several studies have shown the addition of supplemental estrogen during the luteal phase, that after the embryo transfer, improves the pregnancy rates. Generally, we us 4 mg of *Estrace* daily as shown on the protocol flow sheet until the 1st ultrasound exam to document pregnancy.

K. VITAMIN E SUPPLEMENTATION

Some studies have shown that anti-oxidant treatment may improve semen parameters in men with poor sperm counts. Other reports have suggested that vitamin E may aid embryo development in-vitro (in the lab), possibly by reducing oxygen derived free radicals that may be detrimental to embryo growth in culture. We hope to decrease some of the effects of oxidative stress with vitamin E supplementation.

Administration: 800 IU to 1000 IU once a day

4. PROCEDURES-*what to expect.*

OOCYTE RETRIEVAL

The procedure done to remove the eggs from the ovaries is referred to as the "oocyte retrieval". This is an out-patient procedure, performed in our office in the procedure room. The stimulated ovaries generally sit next to the vaginal will, as is easily seen with the transvaginal ultrasound probe. A small needle attached to the probe allows us to aspirate the eggs from the ovaries with minimal discomfort. Patients are given intravenous sedation by the Anesthesiologist (MD), while we continuously monitor ECG, oxygen levels and blood pressure. The Anesthesiologist is present throughout the entire process. The patient is generally deeply sedated breathing on their own and not intubated. Patients generally have no memory of the procedure which lasts about 15 minutes. Our goal is maximum patient comfort. Following administration of the sedation, Dr. Donahue will insert a speculum and cleanse the cervix and vagina. The

speculum is then removed, and the ultrasound probe with needle guide attached is inserted. (A similar ultrasound machine and probe are used for the retrieval as are used in the office to monitor follicle development. Dr. Donahue will identify and examine the uterus, endometrium, and both ovaries. When the ovaries are aligned properly on the ultrasound monitor, Dr. Donahue will introduce the needle through the wall of the vagina and into the first follicle. Suction is applied, and the follicle will be emptied of its contents. The follicle is then refilled, rinsed and emptied again to be sure that the egg has indeed been removed. Normally, each follicle is rinsed three or four times. This process continues until all follicles from that ovary have been emptied. We may not get eggs for all follicles, especially smaller ones. Not all eggs may be mature.

At this point in the procedure, Dr. Donahue will remove the aspiration needle and rinse the collection system completely. The retrieval process will continue with the second ovary.

Oocyte retrieval procedures normally take from 15-20 minutes to complete, depending on the number of follicles to be aspirated. When the second ovary is finished, Dr. Donahue will remove the ultrasound probe and check the cervix and vagina for any bleeding. The retrieval procedure is then complete, and you will be taken to the recovery room. You will be observed by our nurse while the effects of the sedation wear off. You should be ready to go home within one hour after the end of the procedure.

At some point, on the day of the retrieval, the husband will be asked to provide a semen sample. If the two of you want to be together during the collection, please inform your nurse so arrangements can be made for the collection before the wife if prepped for her procedure. This is very much your choice- we just need to know your wishes. Occasionally, if a specific laboratory procedure is being done with the sperm, collection will need to be done at a specific time. If this is the case, one of the biologists from the lab will make you aware of the instructions. You will begin **Progesterone 100mg vaginal suppositories, one every night, starting the day of the retrieval until the morning of the transfer (put the last suppository in the vagina when you first get up on the morning of transfer**). Take the suppositories at night before you go to sleep. Wear a pad in case some leaks out of the vagina. The progesterone will relax the uterus by decreasing the contractions that appear to be frequent during the IVF procedure and may have a negative effect on implantation. **Progesterone in oil shots (2 cc/ml every day**) **and Estrogen support (*Estrace*, 4 mg/day)** will start the day after the egg retrieval. **Progesterone support will continue until 10-12 weeks of the pregnancy and the Estrogen support will be weaned off by 6 weeks of pregnancy.**

AFTER THE RETRIEVAL

In the 24-hour time period following the retrieval, it will be important for you to rest in a semi-upright position. While studies have shown that patients can resume normal activities within 1 hour of an embryo transfer without negative effects, we urge caution and suggest that patients 'take it easy.' When the ovaries are punctured to remove eggs, they ooze bloody fluid for a while until the puncture sites heal over. If this bloody fluid reaches the area of your diaphragm, (as would happen if you laid flat) you may experience some chest and shoulder pain. Plan to sleep in a recliner chair or propped up in bed with pillows on that flat night after retrieval. (you will be given a prescription for

pain medication (*i.e. Demerol*) when you leave the recovery area. Tylenol often works well to relieve post-procedure pain as well; we do request that you not use ibuprofen medications (Motrin, Advil. etc.) for pain relief, however.

In the late morning or early afternoon of the day following retrieval, you will receive a call from the lab regarding your embryo report. We will let you know how many of the eggs have fertilized, and when the embryo transfer is scheduled.

EMBRYO TRANSFER

The procedure to place the embryos into the uterus is referred to as the "embryo transfer". It is normally performed between 3 and 5 days after the egg retrieval. The transfer is done in the procedure room and does not require any sedation or medication.

We will ask you to arrive 30-45 minutes prior to the scheduled procedure and change clothes in preparation for the procedure. You will take the prescribed *Valium 10 mg*, **one hour prior to the transfer time** to help you relax. Additionally, you will place the last *progesterone suppository* in the vagina **when you first get up the morning of the transfer**. This may help the uterus soften and not contract during the transfer procedure. The placement of the embryos into the uterus is done with ultrasound guidance- but this time, the ultrasound will be done abdominally. It will be necessary for you to have a **moderately full bladder** when Dr. Donahue performs the transfer. Plan to **drink 2 to 3 glasses** (8 ounces) of fluid about **an hour before the scheduled transfer time**.

You will be given pictures of you embryos before we do the transfer. Please see other pages on our site for examples. Our embryologists and Dr. Donahue can answer any questions you may have regarding them. At this time, we must decide on the number to transfer based upon the quality of the embryos and other issues we have reviewed before the cycle. Partners are encouraged to be present for the transfer procedure. We have the partner appropriately gowned to be in the clean procedure room with cap and mask. He will be able hold your hand during the procedure. He will also sign some paperwork we have at that time. He will essentially witness the transfer process. Dr. Donahue will cleanse the cervix and vagina similar to the retrieval procedure and then do a 'test pass' of a catheter into the uterus. Once this is comfortably done, he will instruct the biologist in the lab to "load the embryos". At this time, they are removed from the incubators, placed into the transfer catheter, and brought into the transfer room. Dr. Donahue will pass the very slender catheter through the cervix, and guide it to the proper location in the fundal (i.e. mid to upper) area of the uterus. You will be able to watch on the ultrasound monitor as the embryos are expelled from the catheter into your uterus. The laboratory biologist will then check the catheter, under the microscope, to be sure it has been emptied of the embryos. Occasionally an embryo may be retained in the catheter ane we will place it back in the uterus immediately.

In order to give the uterus ample time to calm down, and a chance for the embryos to "settle in", we will keep you here in the office for approximately 20-40 minutes after the transfer. You will need to lie flat for this time.

5. Sample Protocol Calendars.

The following 2 protocols are filled out and reviewed with the patient by Dr. Donahue. We need to generally start birth control pills, if they will be utilized by day 7 of the menstrual cycle. Some patients will not be on birth control to regulate the cycle prior to ovarian stimulation.

PATIENT ______________________ Acct #____________

IVF Long *Lupron* Protocol w/ BCP's

Month #1. *All IVF appt's should be completed before or during this time of taking BCP's*
Begin BCP's on __________. Stop BCP's on _____________.
*****Never** *take the last week (4th week of pills), if necessary you must go into a second pack of BCP's and start with the first pill again!*
Continue taking Prenatal vitamins once daily
Begin mini aspirin (81mg) on _________ until the 12th week of pregnancy
Begin Vitamin E 1000 iu (units) on ____________ once a day until directed
Begin **Lupron 10** iu (units) on _________ (upper thigh or abdomen) once daily until your *actual* cycle day 1- then it drops down to **5** iu

Month #2. ***Call us** on the **actual** first day of your period (Cycle Day 1)!!*
If your cycle falls on the weekend call our office early on Monday morning!

	Estim. (date)	Actual (date)	Lupron (dosage)	FSH (dose)	HMG (dose)	E2/LH/P4 (bloodwork)
Day 1	______	______	________	_____	_____	\ *Baseline US &*
Day2	______	______	________	_____	_____	| *E2 , LH done*
Day 3	______	______	________	_____	_____	/ *on CD1, 2 or 3*
Day 4	______	______	________	_____	_____	
Day 5	______	______	________	_____	_____	
Day 6	______	______	________	_____	_____	
Day 7	______	______	________	_____	_____	*US & bloodwork
Day 8	______	______	________	_____	_____	
Day 9	______	______	________	_____	_____	*US & bloodwork
Day 10	______	______	________	_____	_____	
Day 11	______	______	HCG 10,000 iu/2 cc IM			* US & bloodwork
Day 12	______	______	________	_____	_____	
Day 13	______	______	**Egg Retrieval** (Progest. supp. begin the night of your retrieval)			
Day 14	______	______	Begin Progesterone oil/2cc IM once daily(& Medrol if AH indicated)			
Day 15	______	______				
Day 16	______	______	**Embryo Transfer**			
Day 25	______	______	Progesterone & Estrogen level (llabwork done 1 wk after transfer)			
Day 32	______	______	Pregnancy Test (bloodwork done 2 wks after transfer)			

Notes:
1. Depending on how slow or fast you stimulate with the meds, the calendar dates may change and 1-2 more US's &/or blood work would be needed!
2. On day of HCG, begin Doxycycline 100mg twice a day (am/pm) x 6 days
3. On night of retrieval, begin progesterone vaginal suppositories, 100mg/day when you go to sleep until the morning of the transfer. This will help relax the uterus.
4. Further instructions & teaching of other meds will be reviewed at each office visit and procedure day!! Please call us with any other questions you may have! It's very important to understand and follow this calendar! Thank you!

PATIENT ______________________ Acct #____________

IVF Micro *Lupron* Protocol w/ BCP's

Month #1. *All IVF appt's should be completed before or during this time of taking BCP's*
Begin BCP's on __________. Stop BCP's on _____________.
******Never*** *take the last week (4th week of pills), if necessary you must go into a second pack of BCP's and start with the first pill again!*
Continue taking Prenatal vitamins once daily
Begin mini aspirin (81mg) on _________ until the 12th week of pregnancy
Begin Vitamin E 1000 iu (units) on ___________ once a day until directed

Month #2. ***Call us on the actual first day of your period (Cycle Day 1)!!***
If your cycle falls on the weekend call our office early on Monday morning!

	Estim. (date)	Actual (date)	MicroLup (dosage)	FSH (dose)	HMG (dose)	E2/LH/P4 (bloodwork)
Day 1	______	______	________	_____	_____	\ *Baseline US &*
Day2	______	______	________	_____	_____	| *E2, LH done*
Day 3	______	______	________	_____	_____	/ *on CD1, 2 or 3*
Day 4	______	______	________	_____	_____	
Day 5	______	______	________	_____	_____	
Day 6	______	______	________	_____	_____	
Day 7	______	______	________	_____	_____	
Day 8	______	______	________	_____	_____	
Day 9	______	______	________	_____	_____	* US & bloodwork
Day 10	______	______	________	_____	_____	
Day 11	______	______	________	_____	_____	* US & bloodwork
Day 12	______	______	________	_____	_____	
Day 13	______	______	HCG 10,000 iu/2 cc IM			* US & bloodwork
Day 14	______	______	________	_____	_____	
Day 15	______	______	**Egg Retrieval** Progest. supp. begin the night of your retrieval)			
Day 16	______	______	Begin Progesterone oil/2cc IM once daily & Medrol if the Assisted procedure if indicated			
Day 17	______	______				
Day 18	______	______	**Embryo Transfer**			
Day 25	______	______	Progesterone & Estrogen level (llabwork done 1 wk after transfer)			
Day 32	______	______	Pregnancy Test (bloodwork done 2 wks after transfer)			

Notes:
1. Depending on how slow or fast you stimulate with the meds, the calendar dates may change and 1-2 more US's &/or blood work would be needed!
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