Egg Freezing

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Welcome to the Wisconsin Fertility Institute and thank you for your interest in our Egg Freezing program. This packet is designed to act as a resource for you as you begin the journey through the complex world of assisted reproduction. We have attempted to provide as many answers to your questions as we could anticipate. However, this is not a stand-alone document meant to answer all your questions and concerns; rather, this packet is meant to provide an overview and to supplement information obtained from your doctor, the nursing team, and other members of the Wisconsin Fertility Institute.

Here at WFI, we are firm believers in the partnership between medical team and couple to achieve a goal that is decided upon in a collaborative manner. We do not practice paternalistic directives; nor do we pretend to necessarily know what is always in your best interest. Instead, we will do our best to explain what we prefer to do and why we do it. If you feel confused or pressured, please speak up and let us know as this is not our intent. We strive to create an atmosphere of trust and cooperation, and we can only do that if you are an active member of the team voicing your concerns if you feel your needs are not being met.

We realize that creating a family is a serious endeavor, and that your decision to pursue egg freezing is a commitment to sacrificing considerable time and expense. We also understand how anxiety-provoking the process can be. To this end, we have attempted to minimize stress by providing a safe, comfortable environment. We also have several ancillary services available via local professionals, designed to aid in your ability to cope with the pressure of assisted reproduction. Please ask us about these services.

Once again, thank you for your interest in and support of the Wisconsin Fertility Institute. We sincerely hope to help you build the family of your dreams, and we are honored to have the privilege of working with you.

Gretchen Collins, MD

Meghan Ogden, MD

What is Egg Freezing

Human **oocyte cryopreservation (egg freezing)** is a process in which a woman's eggs (oocytes) are extracted, frozen and stored. Later, when she is ready to become pregnant, the eggs can be thawed, fertilized, and transferred to the uterus as embryos.

History

Cryopreservation itself has always played a central role in assisted reproductive technology. With the first cryopreservation of sperm in 1953 and of embryos thirty years later, these techniques have become routine. Dr Christopher Chen of Singapore reported the world's first pregnancy in 1986 using previously frozen oocytes. This report stood alone for several years followed by studies reporting success rates using frozen eggs to be much lower than those of traditional in vitro fertilization (IVF) techniques using fresh oocytes. Providing the lead to a new direction in cryobiology, Dr. Lilia Kulesiva was the first scientist to achieve vitrification of human oocytes that resulted in a live birth in 1999. Then recently, two articles published in the journal, *Fertility and Sterility,* reported pregnancy rates using frozen oocytes that were comparable to those of cryopreserved embryos and even fresh embryos. These newer reports affirm that oocyte cryopreservation technology is advancing.

Indications

Oocyte cryopreservation is aimed at three groups of women: those diagnosed with cancer who have not yet begun chemotherapy or radiation therapy; those undergoing treatment with assisted reproductive technologies who do not consider embryo freezing an option; and those who would like to preserve their future ability to have children, either because they do not yet have a partner, or for other personal or medical reasons. Over 50,000 reproductive-age women are diagnosed with cancer each year in the United Stated. Chemotherapy and radiation therapy are often toxic for oocytes, leaving few, if any, viable eggs. Egg freezing offers women with cancer the chance to preserve their eggs so that they can have children in the future.

Oocyte cryopreservation is an option for individuals undergoing IVF who object, either for religious or ethical reasons, to the practice of freezing embryos. Having the options to fertilize only as many eggs as will be utilized I the IVF process, and then freeze any remaining unfertilized eggs can be a solution. In this way, there are no excess embryos created, and there need be no disposition of unused frozen embryos, a practice which can complex choices for certain individual. Social egg freezing is a term used to describe the use of egg-freezing as an attempt to delay childbearing in a non-medical context. There has been a proliferation in the marketing of this kind of egg freezing since October 2012 when the American Society for Reproductive Medicine lifted the experimental label from the technology. Additionally, woman with a family history of early menopause have an interest in fertility preservation. With egg freezing, they will have a frozen store of eggs, in the likelihood that their eggs are depleted at an early age.

Method

The egg retrieval process for oocyte cryopreservation is the same as that for in vitro fertilization. This includes one to several weeks of hormone injections that stimulate ovaries to ripen multiple eggs. When the eggs are mature, the final maturation is performed by using a GnRH agonist or human chorionic gonadotropin (hCG). The eggs are subsequently removed from the body by transvaginal oocyte retrieval, a procedure performed under conscious sedation. The eggs are immediately frozen. Eggs are the largest cells in the body, and as such are extremely vulnerable to damage when freezing. Past methodology results in poor survival and pregnancy rates.
However, today eggs are frozen using a flash-freezing process known as vitrification, a huge improvement over older methods of oocyte freezing. Vitrification is associated with higher survival rates and better development compared to older methods.

Success Rates

In a 2013 analysis of more than 2,200 cycles using frozen eggs, scientists found the probability of having a live birth after three cycles was 31.5 percent for women who froze their eggs at age 25, 25.9 percent at age 30, 19.3 percent at age 35, and 14.8 percent at age 40. Two recent studies showed that the rate of birth defects and chromosomal defects when using cryopreserved oocytes is consistent with that of natural conception. In 2014, a scientist's review compared vitrification (the newest technology) versus slow freezing (the oldest one). Key results of that review showed that the clinical pregnancy rate was almost 4 times higher in the oocyte vitrification group than in the slow freezing group.

WHAT ARE THE RISKS ASSOCIATED WITH IVF INCLUDING EGG FREEZING?

The track record of safety for IVF over the years has been very good. Nonetheless, there are risks that you should be aware of:

Ovarian Hyperstimulation: The fertility drugs used in IVF usually cause the ovaries to enlarge somewhat. Some women's ovaries are so sensitive to these medications that they enlarge 4- or 5-times normal size and cause discomfort and leakage of fluid from the blood vessels into the abdomen, a problem called Ovarian Hyperstimulation Syndrome (OHSS). Severe OHSS occurs in less than 1% of patients but usually requires hospitalization and careful treatment to avoid you getting very sick. The hospital stay can sometimes be several weeks, particularly if you are pregnant.

We minimize the risk of severe OHSS by carefully monitoring your progress during drug treatment and adjusting the drug doses as necessary.

Infection: There is a 0.1 percent (1 per 1,000) risk reported in the medical literature that a pelvic infection would occur after egg retrieval. These infections have been mild in some cases and severe, even to the point of requiring major surgery, in others. We always attempt to minimize this risk by using sterile techniques and treating you with antibiotics.

Cancer**:** A study in 1994 showed a possible increase in the risk of ovarian cancer in women who took the fertility pill clomiphene citrate (Clomid) for a long period of time (12 or more months). Clomid is rarely used in IVF, and no studies to date have indicated any increased risk for other IVF medications, but perhaps studies in the future will. However, given the difficulty of demonstrating an increased risk of ovarian cancer despite nearly 30 years of IVF, it is likely that even if the risk is increased it is a slight increase! Counterbalancing this theoretical risk is the known benefit of pregnancy, which substantially lowers the risks of cancer of the breast, ovary and uterus.

Steps to Begin Your Egg Freezing Cycle

New Patient Phone Consult with Provider- You will discuss previous medical history and treatment plan.

Lab orders to complete the necessary testing for your IVF cycle.

- AMH
- TSH
- Blood Type*
- Rubella and Varicella Titer*
- Infectious Disease Testing

The testing can be completed at LabCorp or with your own provider. Please call them to confirm how to best complete the testing within their system and to ensure the results are sent over to our office as soon as they are completed.

All labs must have been completed within the last year except for Rubella/Varicella Titer and Blood Type. If you have had any of the other tests completed within the last year, it is not necessary to repeat them. Simply have the results sent to our office.

Once labs are completed and received, you will receive a call from our Coordinator to discuss the next steps. These include:

- *Treatment Plan visit with your doctor.*
- *Injection Training-Completed online through our website*

Please do not hesitate to call us or reach out through your patient portal if you have any questions or concerns along the way. We look forward to working with you!

Financial Counseling Appointment *Required*

During your financial counseling appointment, you will meet with one of our finance team members to discuss your treatment cost, payment schedule, financing options and consent forms. We will also be able to answer any questions you may have during this time regarding cost and consents. Please understand that no medications will be ordered, and you will not be able to proceed with your treatment until this call is completed and consent forms are returned.

You will receive consent forms and your estimates ***via your patient portal*** after your New Patient consultation with the provider. Once you have received these you may schedule your financial consultation online through your patient portal.

Login to your patient portal
Choose Appointments
Click on the green Make an Appointment button at the top of the page
Continue to Select a Day
Simply choose the day and time you would like to have your call.
On the day of the call the Finance team will call you.

We look forward to joining you on this journey!

Cycle of Treatment

There are several different approaches to drug administration for egg freezing treatment cycle, and each has been found to be the best approach in some patients. However, no approach works for everyone, and occasionally a poor response to medication may necessitate a discontinuation of treatment, with resumption later using a different drug combination. In this center, three approaches are used primarily, although small variations may sometimes occur for individual patients:

Antagonist: This is the most common regimen that is currently used. With the beginning of the menstrual period, a baseline visit is conducted. This visit consists of three steps: (a) an ultrasound to show that nothing has begun to grow on the ovaries, (b) a blood estrogen level to confirm that nothing was missed on ultrasound, and (c) a check to make sure consent has been obtained. If the ovaries are quiet, the estrogen level is low, and consent forms are signed, we are ready to begin stimulation of the ovaries. Follistim or Gonal F is begun on this day and continued for 9-14 days. It is given subcutaneously (SQ), (small needle just under the skin). Periodic ultrasound examinations and blood estrogen levels are performed. When the largest ovarian follicle (egg surrounded by fluid) measures 14 mm, daily injections of Cetrotide or Ganirelix are administered SQ each morning until many eggs are fully grown and mature. The drugs are then discontinued and either Ovidrel/Lupron or a combination of both (trigger shots) is administered to allow the retrieval of the eggs. These SQ drugs are given 36 hours before harvesting your eggs and is responsible for their final maturation and readiness to be mixed with sperm.

Agonist suppression: With this approach, women begin a drug called Lupron after a couple of weeks on oral contraceptives. The drug is administered daily by SQ injection. When a subsequent period begins, the woman comes to the clinic for a baseline visit. The Lupron is continued Follistim or Gonal F is added each day for 9-14 days total. Once the eggs are mature you will take the trigger shots 36 hours before egg harvesting.

Microdose flair: In patients with a previous poor response to stimulation, who are age 40 or over, or who have a day 3 FSH value over 10, or an AMH less than 1.5, another approach to stimulating the ovaries is Microdose Flair. The idea behind this treatment protocol is to use the body's own FSH in combination with Follistim or Gonal F to stimulate the ovaries to grow eggs. The day after your period begins you have a baseline visit, and if all is acceptable you administer a low dose of Lupron subcutaneously twice daily. After the first 2 days of Lupron, Follistim or Gonal F are added at a dose of 450 units daily. This is continued, with periodic ultrasound examinations and blood estrogen tests, until a reasonable number of eggs have grown and matured (usually 9-14 days). The previous drugs are then discontinued and 2 Ovidrel (trigger shots) are administered to allow the eggs to be retrieved.

Medications Often Involved

Follistim/Gonal-F/Menopur: These drugs are used to help grow eggs. They are the same hormones that your own body makes to grow eggs. Your own body will secrete a small amount of this hormone during your menstrual cycle, so that you grow one mature egg. You will take high doses of these hormones to grow extra eggs in a cycle. You usually will take these drugs for 9-14 days during your treatment. These drugs are injected just underneath the skin in your belly or your thigh.

Omni trope: This drug is another shot taken just underneath the skin. It is used for women that may need a little extra help to improve quality of their eggs.

Ovidrel/Novarel/Lupron: These shots, taken just underneath the skin, are used as trigger shots to prepare the eggs for retrieval. The timing of these particular shots is CRITICAL.

Ganirelix/Cetrotide: These drugs are also given as shots, just underneath your skin in your belly or thigh. It is usually taken in the morning and is used to stop your eggs from ovulating too early.

Estradiol/Estrace: This drug is given by mouth and will begin once you start growing your lining for a frozen embryo transfer. You will continue it until week 11 gestation or until you have a negative pregnancy test.

Progesterone: This drug is after the lining check during your frozen embryo transfer. It helps keep the uterine lining thick and helps improve implantation of the embryo. You will continue it until week 11 gestation or until you have a negative pregnancy test.

Doxycycline: This is a drug taken by mouth that decreases infection rates. You will take it twice a day beginning the day of the retrieval.

Prednisone: This medicine can increase implantation rates by suppressing the immune system. This is used during the frozen embryo transfer cycle.

Valium: This medicine is taken at the time of the embryo transfer to help relax the uterine muscle.

Lovenox: This drug may be used in your embryo transfer cycle. It is given just under the skin as a subcutaneous shot to help with embryo implantation.

Transvaginal Oocyte (Egg) Retrieval

Thirty-six hours after the administration of the trigger shots, you will undergo a procedure called egg retrieval. You will be instructed not to eat or drink anything after midnight the night before the egg retrieval, and the morning of the retrieval, due to the anesthesia given. You will need a ride home that day. On the day of the retrieval, a fresh semen sample will be obtained for use in the fertilization process. In certain situations, a sample can be obtained earlier and cryopreserved or frozen. The specimen would then be then thawed for use on the day of retrieval.

The egg retrieval procedure is done at our office under light anesthesia (intravenous sedation). A needle guided by ultrasound is passed through the top of the vagina and into the follicles in the ovary. It takes about 30 minutes to retrieve the eggs, and then 60-90 minutes to rest in our recovery room. The fluid we remove from the follicles is given immediately to our embryologists who use their microscopes to find the otherwise invisible eggs. The eggs are usually inseminated a few hours after retrieval with sperm from your husband, partner, or an anonymous sperm donor. This is done by our embryologists who are also responsible for culturing the fertilized eggs (now called embryos) until the time of transfer to your uterus. The day of retrieval you will begin an antibiotic called doxycycline (2 times daily) which will help decrease risk of infection. You will continue taking this drug for 5 days.

Risks of Egg Retrieval

Infection: Bacteria from the vagina may be transferred into the pelvis or ovaries by the needle. This can cause an infection of nearby organs. The incidence of infection after egg retrieval is small (less than 0.1%). If you do get an infection, you may be given antibiotics. Severe infections sometimes require surgery to remove infected tissue. Infections can reduce your chance of getting pregnant in the future. Antibiotics may be used before the egg retrieval to help reduce the chance of infection. Still, there is no way to remove the risk completely.

Bleeding: The needle passes through the vaginal wall and into the ovary to obtain the eggs. Both structures contain blood vessels. There are also other blood vessels nearby. This means that tiny amounts of blood may be lost while removing the eggs. The risk of major bleeding is small (< 0.1%). Major bleeding may require surgery to stop and could result in the removal of an ovary. Only rarely is a blood transfusion needed. If bleeding occurs and is not noticed (also rare), it can lead to death.

Trauma: Even with ultrasound guidance, nearby organs can be damaged. This includes damage to the intestines, appendix, bladder, ureters, and ovary. In some cases, a damaged organ may need to be fixed or removed through surgery. Still, the risk of damage during egg retrieval is extremely low.

Anesthesia: The use of anesthesia while removing eggs can cause an allergic reaction or low blood pressure. It can also cause nausea or vomiting. In rare cases, use of anesthesia has resulted in death.

Failure: Sometimes no eggs are found during the retrieval process. In other cases, the eggs are not normal or are of inferior quality. These situations can prevent you from having a successful pregnancy.

Timing of Medications for Egg Retrieval Process:

Please let the office know on day 1 of the month prior to starting egg freezing cycle that you are interested in egg freezing the following month. They will schedule you for a luteal progesterone level (around day 21). You may do an IUI (intrauterine insemination) this cycle if that is part of your treatment plan. If your progesterone level is appropriate, you will be started on estrogen three times a day (estrace 3mg TID).

On day 1 of your next menstrual cycle, you will call the office to set up your baseline visit. If it is a weekend or after hours, call the office the following business day. You will stay on the estrace and this will prevent you from starting another cycle and keep all the follicles in the ready position for stimulation. Depending on your cycle you may be on the estrace for 1-14 days prior to starting the IVF stimulation medications.

The nurses will let you know when you will come in for your baseline visit. During this visit, we will perform 1) a blood test and 2) an ultrasound exam of your uterus and ovaries to make sure there are no cysts and that all the eggs are small.

If your lab levels are appropriate, your ovaries have no large eggs, and your uterus looks ready, you will be instructed, to start the first set of drugs to grow the eggs and some that will improve egg quality.

Over the next 12-14 days, you will come in for ultrasound examinations and blood draws. You will be seen somewhere between 4 and 7 times during this 2-week period. We will adjust your dosing of drug to grow the eggs during this process.

About midway in the cycle, you will add the drug that will stop you from ovulating (Cetrotide, Ganirelix). These drugs are taken in the mornings, for 5-7 days total.

When your eggs are mature, (at least two of them measure about 20 x 20 mm average size) you will be told to stop taking the previous drugs. That evening you will take your trigger injection(s): Ovidrel/Lupron/Novarel. The trigger will allow the eggs to mature even further.

You will be given a specific time to take this medication—the trigger injection(s) must be given within fifteen minutes of the time you are told to inject!

The next day is the day before your retrieval. It is a shot free day.

You may not have anything to eat or drink after midnight the day before the retrieval.

Retrieval Day

The retrieval is performed 36 hours after you have taken your trigger shot. You should not eat or drink anything after midnight the night before the retrieval. If you usually take medications in the morning, it is ok to do so with a tiny sip of water.

When you come to the clinic, we will place an intravenous tube into a vein in your arm. We will give you drugs for conscious sedation; you will be a little sleepy and won't feel any pain.

During the retrieval, an ultrasound is placed into your vagina, and we aspirate or extract the eggs by passing a small needle across the vagina and inserting it into the ovary while we watch with the ultrasound. We will remove all eggs found if you are undergoing standard IVF. Keep in mind that ultrasound is a guide, sometimes we get more eggs than expected and sometimes we get less. If we get a much lower number of eggs than expected, that can indicate poor egg quality. This can either be a contributing factor to your subfertility or may have been a bad batch of eggs. You will have sedation and thus will need someone to drive you home after the procedure.

Cryopreservation

Some women may wish to freeze their eggs because they are not ready to conceive now, or because they are planning to have therapy such as cancer treatment that could damage their eggs.

Benefits of Freezing:

- Saves you from going through ovarian stimulation again if you need eggs or embryos in the future.

There are different ways to freeze eggs. The most common are "slow "freezing and "rapid" freezing (called *vitrification*). You should know that eggs do not always survive the freezing and thawing process. There is always a risk that no eggs will survive.

Storage Fees

Once your eggs are frozen at WFI, you will be responsible for the yearly storage fees. If you choose to freeze your eggs with us, you will need to fill out a credit card authorization form to set up automatic billing. Each time you freeze a new batch of eggs, you will be billed separately each year for that batch. The cost of egg storage is $400.00 per year. Should you discontinue storage before the year ends, you will not be given a refund. This storage fee will be charged yearly until all eggs have been used or discarded.

Frequently Asked Questions

I have had all my lab testing done. Now what do I do?

If your testing was completed at the Wisconsin Fertility Institute, we will contact you when the results are in and have you set up an appointment with one of the providers to discuss your specific treatment plan. If your testing was done through your own health care provider, call us if you need our help getting the results sent or faxed to our office. Once we have received all the records, we will contact you to set up your treatment plan visit.

When is day one of my menstrual cycle?

This can be difficult for some people to know if they are spotting or bleeding stops and starts. Day one is considered the first day you see **flow.** Spotting does not count as flow. If you are not using a pad or tampon, then it is not day one yet. If you are unsure about what day counts as day 1, call us!

I need a refill on one or more of my medications. What do I do?

When we call in your original prescription, we also call in several refills. Simply contact the pharmacy from where you received your original prescription, and they will mail out more medications. Some pharmacies do not deliver on the weekends, so if you need more medication on Saturday or Sunday, you should have it delivered by Friday. If you need help, feel free to call us.

The flow sheet on the patient portal doesn't tell me which dose of medication to take tomorrow. What do I do?

When looking on the patient portal Flow sheet Tab, you will notice the medications are listed for each day you are to take them. You can look at the Patient Instructions tab to see when your next ultrasound and estrogen appointment should be scheduled. If you are still having trouble, call us!

What time of day should I take my medication?

- **Follistim/Gonal-f/Stimulation Drugs**: We usually prefer you take these in the afternoon/early evening.
- **Omnitrope**: this is also taken in the evening with the evening drugs.
- **Cetrotide/Ganirelix**: this medication is taken in the mornings, make sure you take it within 30 minutes of your scheduled time each morning. You will still take this medication the day that you trigger with Lupron or Ovidrel in preparation for the egg retrieval.
- **Lupron/Ovidrel/Novarel AS A TRIGGER:** These medications should be taken at the precise time that we tell you. Your egg retrieval time is based on when you took these trigger shots, so taking them on time is important. If you take your trigger shot at another time than we indicated (by more than 15 minutes) please call us right away.
- **Progesterone:** Should be at the same time each day, once daily, sometime in the morning.
- **Doxycycline:** Every 12 hours/twice daily with food.
- **Estrogen/Estrace:** This drug can cause nausea, so it is best to spread it out during the day. You can take it with meals or at bedtime. It will be taken 4 times daily.

Which medications should be refrigerated, and which ones should be kept at room temperature? When do they expire?

Please see the Medication Storage Fact Sheet in your Egg Freezing folder for a complete listing of medications and instructions.

What about herbs, supplements, or over the counter medications?

Any medications besides the ones we are prescribing should be cleared by one of our staff. Please review all medications you take with us. Tylenol and Benadryl products are ok to use during the cycle. Ephedrine based medications should be avoided

MEDICATION STORAGE INFORMATION

Cetrotide 0.25mg - Store refrigerated. Store in original box. Use immediately after reconstitution/mixing.

Crinone 8% Vaginal Gel - Store at room temperature. It is acceptable to store at slightly lower or higher temperatures for very brief periods of time (as low as 59°F and as high as 86°F).

Endometrin lOOmg Vaginal Inserts - Store at room temperature. It is acceptable to store at slightly lower or higher temperatures for very brief periods of time (as low as 59°F and as high as 86°F).

Follistim AQ Cartridge 300IU, 600IU, 900IU - Store refrigerated until the expiration date OR at room temperature for 3 months or until expiration date, whichever occurs first. Once the Cartridge has been pierced by a needle, it can be stored for a maximum of 28 days refrigerated or at room temperature. Protect from light. Do not freeze.

Ganirelix 250mcg Syringe - Store at room temperature. It is acceptable to store at slightly lower or higher temperatures for very brief periods of time (as low as 59°F and as high as 86°F). Protect from light.

Gonal-f 75IU Vial - Store at room temperature or refrigerate until expiration date. Do not freeze. Protect from light. After reconstitution/mixing: Use immediately. Discard unused material. Do not store drug in the syringe.

Gonal-f Pens 300IU, 450IU, 900IU - Before first use: Store refrigerated until expiration date OR at room temperature for up to 3 months or until expiration, whichever occurs first. After initial use: Store at room temperature OR refrigerate for up to 28 days. Protect from light. Do not freeze.

Leuprolide (Lupron) 14-day kit or prefilled syringe- Store refrigerated. Do not freeze. Protect from light.

Menopur 75IU Vial - Store at room temperature or refrigerated. Protect from light. Use immediately after reconstitution/mixing. Discard unused material.

Microdose Leuprolide/Leuprolide Dilution Vial - Keep refrigerated. Do not use after expiration indicated on vial.

Novarel 5,000- or 10,000-Units Vial - Store at room temperature. It is acceptable to store at slightly lower or higher temperatures for very brief periods of time (as low as 59°F and as high as 86°F). After reconstitution/mixing: Refrigerate and use within 30 days.

Ovidrel 250mcg Prefilled Syringe - Store refrigerated until expiration date OR at room temperature for not more than 30 days. Protect from light. Do not freeze.

Progesteronction - Store at room temperature. Do not refrigerate.

Important Information

Website- Patient portal and educational videos**:** **https://wisconsinfertility.com/**

Clinic Phone Number: 608-824-0075 **Fax Number:** 608-829-0748

Address: 3146 Deming Way Middleton, Wisconsin 53562

Clinic Hours: Monday, Tuesday, Thursday and Friday 7:30am-4pm
Saturday and Sunday 8am-9am

Clinical Staff:

Kelly, RN. Charge Nurse

Beth, RN. Egg Donor Coordinator, IVF Nurse

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Ashlee, RN. IVF Nurse