



Egg Freezing

Wisconsin Fertility Institute
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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 the stress by providing a safe, comfortable environment. We also have a number of 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.

Elizabeth A. Pritts, M.D.

Gretchen E. Collins, M.D.

A BRIEF HISTORY OF *IN-VITRO* FERTILIZATION

Robert Edwards, a Ph.D. physiologist, and Patrick Steptoe, a gynecologist, pioneered IVF in Great Britain during the 1970's. Edwards had spent the 1960's working with bits of human ovaries removed at surgery and had achieved the first fertilization of a human egg outside the body in 1967. During these same years, Steptoe was helping to develop the new surgical technique of laparoscopy. By 1971 the two men had met and begun to collaborate. Initially they retrieved eggs from the ovaries of volunteers by laparoscopy and focused on improving the timing of egg retrieval and *in-vitro* culture conditions. By the mid-1970's they felt ready to attempt pregnancy. Their initial pregnancy was, unfortunately, a tubal pregnancy (ectopic) in 1976. Then came true success and the first IVF baby, Louise Brown, was born in July 1978.

Steptoe and Edwards' original group of patients had undergone "natural IVF", meaning they were not given fertility drugs. Instead they were monitored closely and when ovulation appeared imminent, even if it was 3:00 AM, a laparoscopy was done and an attempt made to aspirate the single mature egg. As might be suspected, they didn't always obtain the egg. Two Australian groups were only two years behind in achieving IVF pregnancies but they chose a different route. They stimulated their patients with fertility drugs in hopes of recovering more than one egg. As their initial success rates, about 5% per attempt, were higher than that of Steptoe and Edwards, all subsequent new IVF programs also used "stimulated IVF". Eventually Steptoe and Edwards adopted this approach as well.

The 1980's saw continued improvement in embryology culturing techniques, refinements in fertility drug protocols, and the ability to retrieve eggs with a vaginal ultrasound probe instead of laparoscopy. As a result, IVF success rates began to climb slowly but steadily, reaching 20-25% per attempt for women under the age of 40 by the end of the decade.

The 1990's have seen additional improvements in the process, such as better treatment protocols for women 40 years of age and older and the development of ICSI (Intracytoplasmic Sperm Injection), a revolutionary treatment for severe male factor problems. With ICSI, a single sperm can be injected into an egg and thereby achieve fertilization. For women 35 years of age and older, a technique called Assisted Hatching and the ability to grow embryos longer (3 to 5 days before transfer) have helped improve the odds. Also, the process of egg donation (IVF using eggs donated by a younger woman) was perfected, producing high pregnancy rates in previously hopeless situations.

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 particular 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 States. 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 in 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 individuals.

Social egg freezing is a term used to describe the use of egg-freezing as an attempt to delay child-bearing 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 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 technique 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.

PRE-CYCLE TESTING FOR EGG FREEZING

Test	Description
AMH	Blood test done to check the ability of the ovaries to respond to fertility medication and to determine the ovarian reserve
HIV	Test for HIV infection
VDRL/RPR	Test for syphilis
Hep B S Ag	Test for Hepatitis B
Hep C Ab	Test for Hepatitis C

THE TREATMENT CYCLE FOR EGG FREEZING: A COMPLETE GUIDE

Evaluation and Preparation Phase

You will begin the road to egg freezing by consulting with one of the doctors at the Wisconsin Fertility Institute. At that visit, the doctor will review all treatment options available to you, as well as their likelihood of success and approximate cost. The doctor may also suggest additional tests to further refine the likelihood of success with each option. If you should then opt for egg freezing, you will complete the blood tests above. Once these tests are completed and we have the results, you will again meet with your doctor, review the test results and, if all are normal, proceed to treatment. If one or more tests is abnormal this will be discussed with you and treatment plans reconsidered.

Cycle of Treatment

There are a number of 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 in 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:

- (1) **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 a large number of 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.

- (2) **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.

- (3) **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.

Egg Retrieval

Thirty six hours after the administration of Ovidrel, Lupron or a combination of both, 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 also the morning of the retrieval, due to the anesthesia given. You will need a ride home that day.

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 will be frozen shortly after retrieval.

The day of retrieval you will begin an antibiotic called doxycycline (2 times daily) which will help decrease risk of infection. You will continue this drug for 5 days after the retrieval.



The following is a list of steps to complete before beginning an Egg Freezing cycle:

1. Call the clinic (608-824-0075) to schedule a consultation with one of our doctors.
2. Obtain lab orders to complete the necessary testing for your IVF cycle.
 - AMH
 - Infectious Disease Testing

The testing can be completed here in our office 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 faxed or sent over to our office as soon as they are completed.

All labs must be completed within the last year. Simply have the results sent to our office. Once labs are completed, you will receive a call from our IVF Coordinator to schedule the following appointments:

3. Treatment Plan visit with your doctor
4. IVF Lecture and Injection Training Class

This class is required and takes place in our office every Tuesday and Thursday at 1:30 pm. There is no additional cost for this class.

Once all of the above steps have been completed, you are ready to begin your journey.

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

Egg Freezing: 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 of 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 to know for some people, 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 will 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/Menopur: Stimulation Drugs:** We usually prefer you take these in the afternoon/early evening.
- **Novarel:** this is usually taken in the evening with the Follistim or Gonal F (if prescribed for you).
- **Omnitrope:** this is also taken in the evening with the evening drugs (if prescribed for you).
- **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 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 the time you take the trigger shots, so taking it on time is important. If you take your Lupron or Ovidrel at another time than we indicated (by more than 15 minutes) please call us right away.
- **Doxycycline:** Every 12 hours/twice daily with food.

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.



Egg Freezing 101: A Primer

The following information is intended to give you an overview of the IVF process at Wisconsin Fertility Institute.

Medications Involved with IVF:

Follistim/Gonal-F/Novarel/Menopur: These drugs are used to help grow eggs. They are actually 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.

Omnitrope: 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/Lupron/Novarel: 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.

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.

Timing of Medications in Egg growing:

On day 1 of your menstrual cycle, you will call the office to set up your baseline visit for day 2. If it is a weekend, call the office and have the doctor paged so we can get you set up for your cycle.

On day 2 of the cycle, you will come in for your baseline visit. At this visit, we will perform 1) a blood test to make sure your estrogen level is low and 2) an ultrasound exam of your uterus and ovaries to make sure there are no cysts and that all of the eggs are small.

If your estrogen level is low, 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 perhaps some that will improve egg quality (Gonal-F, Follistim, Menopur and/or Omnitrope).

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) and *maybe* a drug to increase growth rate of the eggs (Novarel). Cetrotide or Ganirelix will be 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): either Ovidrel, Novarel or Lupron or a combination. 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.**

The Retrieval:

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 of the eggs we find.

All eggs will be passed to the Laboratory Director who will look at each egg and freeze all of the mature eggs.



This is an estimate only and prices may vary. This estimate represents the most common charges. Prices may vary depending on your individual care.

Egg Freezing Cycle

	Procedure	Quantity	Cost	Charge
Monitoring:	Ultrasound, Follicular	5	\$ 175.00	\$ 875.00
	Clinic Visit	5	\$ 75.00	\$ 375.00
	Venipuncture	5	\$ 25.00	\$ 125.00
	Estradiol Blood Test	5	\$ 100.00	\$ 500.00
	Progesterone Blood Test	5	\$ 100.00	\$ 500.00
Retrieval:	Egg Retrieval	1	\$ 1,625.00	\$ 1,625.00
	Egg Retrieval Needle	1	\$ 125.00	\$ 125.00
	Egg Retrieval Ultrasound	1	\$ 250.00	\$ 250.00
	Oocyte Identification	1	\$ 900.00	\$ 900.00
	Cumulus Removal	1	\$ 300.00	\$ 300.00
	Procedure Room Charge	1	\$ 400.00	\$ 400.00
	Anesthesia	1	\$ 400.00	\$ 400.00
	Cryopreservation up to 6 eggs	1	\$ 500.00	\$ 500.00

Estimated Prepayment Due: \$ 6,875.00

Please note: prescription drugs are not included in this estimate and generally cost \$5000-\$7000

Payment is due in full at your baseline ultrasound appointment.

Additional services, not included in above estimate, that may be provided in association with IVF cycles:

Cryopreservation of more than 6 EGGS \$500 for up to 6 more eggs
Storage Fees \$400.00 per year or \$55.00 per month

I understand that this is an estimate only and charges may vary depending on services rendered.

Sign: _____ Print: _____ Date: _____

Clinic Representative _____ Date _____