EFG_V2_US

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Introduction

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. . Throughout this series, we'll guide you through the processes and procedures utilized in a freeze-all egg retrieval cycle commonly known as egg freezing.. We'll provide you with in-depth information about the risks, benefits, and choices involved in your treatment program. Patients who understand the overall process tend to have a more positive experience as they progress through the cycle.

We'll cover a lot of ground, so take your time and feel free to repeat videos if there's anything you don't understand. We hope that after you complete this module that you'll feel confident discussing any further concerns with your medical team. . .

Deciding to Freeze Your Eggs

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There are a variety of reasons to pursue egg freezing, but one of the most common is to preserve your fertility. If you were assigned female at birth, you were born with all of the potential eggs, or oocytes, you will ever have, which is generally between 1 and 2 million. Over time, the number of potential eggs in your ovarian reserve declines. By age 18, only about 200,000 eggs remain. A steeper decline usually begins around age 35 as menopause approaches. By menopause, typically only a few hundred eggs remain. Egg quality also decreases over time. This means that as you get older, your chances of getting pregnant decrease, even if you still have a high number of eggs in your ovarian reserve. For those under age 30, the average likelihood of achieving pregnancy is 25% per cycle.. For those over age 30, that likelihood drops to 20% each cycle, and by age 40, conception is as high as 10% per cycle.. This is because of the natural reduction in quantity and quality of eggs over time. Egg freezing allows you to preserve your own eggs when they are young and healthy. It is often recommended for patients to freeze their eggs before receiving treatment that may cause premature infertility or if they choose to delay pregnancy. Although not a guarantee, egg freezing can greatly increase chances of achieving a pregnancy later in life. If you choose to pursue egg freezing, you will first meet with a specialist to determine if Egg Freezing is right for you. This will include screening tests such as **bloodwork** and **ultrasounds**, as well as a conversation about the **optimal number of eggs** you should freeze based on your **age, ovarian function**, and the **number of cycles** it will require to pursue your family planning goals.. In comparison to a fresh IVF cycle, using frozen eggs does not seem to have any adverse health effects. . . .

The Menstrual Cycle

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Before you begin fertility treatment it's helpful to understand the menstrual cycle. Learning about the similarities and differences between the two can help you feel more comfortable with how fertility treatment works. The menstrual cycle is regulated by a fascinating series of coordinated hormonal changes throughout the body. A part of the brain called the

hypothalamus produces a hormone known as gonadotropin releasing hormone, or GnRH, which stimulates the pituitary gland. The pituitary gland then releases two Gonadotropin hormones: follicle stimulating hormone, or FSH, and Luteinizing hormone, LH. In the first half of the menstrual cycle, or follicular phase, the ovary is populated by small fluid-filled structures called follicles, which produce estrogen and contain an immature egg. FSH from the pituitary gland stimulates the growth of a single follicle in one ovary. This happens over about 14 days, causing the follicle to produce more estrogen, and the egg within that follicle to mature. Once the follicle is fully mature and the estrogen level high, production of LH rises sharply completing maturation of the egg and triggering ovulation. Ovulation is the release of an egg from the ovary into the fallopian tube, where sperm traveling through the reproductive tract can find the egg and fertilize it. The sperm must do so within about 24 hours of ovulation or the egg will degenerate and pregnancy will not occur. As you progress through this module, you will see that all of the hormones that are produced in a typical menstrual cycle are also used in fertility treatment, often in higher quantities to increase the number of eggs that may be produced in any one cycle, to improve your chances of successful treatment.

Controlled Ovarian Stimulation: The Process

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To begin treatment, fertility clinics often use medications that stimulate the ovaries to produce multiple eggs at once in a process known as Controlled Ovarian Stimulation, or COS. The goal of COS is to increase the number of high quality eggs for use in fertility treatment. It's helpful to think of the controlled ovarian stimulation process in three phases: suppression, stimulation, and trigger. First, let's look at the suppression phase. This phase may or may not be required, or may overlap with the next phase depending on your specific clinical situation. During this phase, medication is used to suppress the typical production of hormones in order to prevent the development of a single follicle, preparing the ovaries to grow multiple follicles of a relatively even size in the next phase. This also allows your medical team to schedule a cycle. . . To establish a baseline, your medical team will perform hormonal blood work and ultrasound scans. Typically, hormone levels will be low, the endometrial lining will be thin, and the follicles will be small. If everything is as expected, you will progress to the stimulation phase. In the stimulation phase, you'll undergo daily injections of Gonadotropin medications. Your medical team will carefully determine the amount and type of FSH and LH to use based on your medical history and ovarian reserve, in order to produce the optimal number of eggs desired for the cycle. The stimulation phase will usually take between 8 and 14 days, during which time you will be monitored to assess your body's response to the medication. At each monitoring visit, your team may draw blood and measure your estrogen level on a specialized hormone assay machine. As the follicles develop and mature, they will produce more estrogen; your estrogen level will reflect the number and maturity of the follicles and the eggs inside..... Internal sonograms at monitoring visits also help your medical team visualize the number and size of the growing follicles in the ovary. The developing follicles are measured in 2 dimensions and grow approximately 1 to 2 millimeters every day. . The majority of follicles over 15-16 mm will contain a mature egg, and the largest will usually measure above 17 millimeters. By the end of the stimulation process, a good response produces about 8 to 20 follicles, each measuring between 12 and 22 millimeters. However the number of follicles produced can vary from 0 to as many as 50 based on ovarian function, medication dosage, and the protocols used. If an optimal number of follicles does not develop, your medical team may consider canceling this cycle. The likelihood of cancellation increases with advancing age. For people under 35, around 5% of cycles are canceled. This number increases to 15-20% for people older than 42. If this cycle is canceled, your medical team will talk to you about trying different protocols or treatments.. The final stage of the controlled ovarian stimulation process is the trigger injection which is administered once the largest follicles reach the optimal size. . This trigger shot completes the final maturation of the eggs, allowing egg retrieval to be performed 35 to 37 hours later. In some cases, your doctor may wish to check hormone levels the day after the trigger injection to ensure it was effective.

. Throughout the entire controlled ovarian stimulation process, the uterine lining slowly thickens and by the time the follicles reach full maturity, you'll be ready for Egg Retrieval..

Controlled Ovarian Stimulation: The Drugs and Protocols

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There are various medications and protocols that may be used for controlled ovarian stimulation. Some people are anxious about the injections required, but rest assured, this anxiety is completely natural. You may choose to administer the shots yourself, or you may choose to have a friend, family member, or partner perform the injections for you. The medications needed will vary depending on your clinical situation. Your medical team will select the specific protocol and medications required for each phase. Oral contraceptive pills, commonly known as birth control pills, are frequently used during the suppression phase to decrease hormone production or to schedule a cycle. Possible side effects of the pill include irregular bleeding, headaches, chest tenderness, nausea, and swelling. In extremely rare cases, they can cause blood clots or a stroke.

. During the stimulation phase,hormone drugs called gonadotropins will be used to stimulate the ovaries to grow multiple eggs simultaneously. Both FSH and LH are gonadotropins, which are produced by the pituitary gland during a typical menstrual cycle. FSH can be administered by subcutaneous injection, which means that the needle used is very short and the injection occurs under the skin, rather than into the muscle. Overall, FSH drugs are well tolerated, however, there are infrequent side effects, including: fatigue, headaches, nausea, mood swings, or rarely: clots in blood vessels. Temporary weight gain of between 2 and 5 pounds may also occur due to fluid retention. As with any medicine taken as an injection, mild injection site reactions, such as bruising, irritation, or redness, can occur. Clomiphene Citrate, commonly referred to as Clomid, and Letrozole, are oral tablet medications that work by increasing the amount of FSH and LH released. Clomiphene citrate is usually very well tolerated and side effects are mild and infrequent; however, a small percentage of people may experience dizziness and other visual symptoms which could be serious. Letrozole, while not currently cleared by the FDA for fertility use, has minimal side effects even when compared to Clomid.

. Another type of injectable medication, known as GnRH-antagonists, are usually given to patients mid-cycle as the follicles start growing to prevent premature ovulation... GnRH-antagonists are typically well tolerated, but can produce mild local injection site reactions, abdominal pain, headaches, and nausea...... GnRH-agonists, not to be confused with GnRHantagonists, initially stimulate the pituitary gland to release FSH and LH, but after a few days of continuous use, they have a suppressive effect. This means, they can be used for various purposes throughout the different phases. Your doctor might prescribe GnRH-agonists to start the growth of eggs, to suppress premature ovulation, or as a trigger shot to complete the final maturation of the eggs. One commonly used GnRH-agonist is called Leuprolide-Acetate, or Lupron. Lupron is FDA-approved for a variety of medical conditions and although not specifically approved for fertility treatment, it has been used in fertility treatment for over 20 years. When GnRH-agonists are used in ovarian suppression, patients may experience a few days of menopausal-like side effects, such as: headaches, hot flashes, muscle aches, and a depressed mood. When used as a trigger shot, these side effects are very rare.. hCG, or Human Chorionic Gonadotropin, is often prescribed as the trigger injection to complete the final maturation of the developing eggs before retrieval. hCG acts in a similar fashion to the LH surge that occurs in the non-medicated menstrual cycle. The trigger drug is either administered by subcutaneous injection using a very small needle, or as an intramuscular injection given in the gluteal muscle. Side effects of HCG may include chest tenderness, bloating, and pelvic discomfort.. Because all patients are unique, your medical team will select protocols and dosage based on many factors, including age, weight, previous response to medication, blood hormone levels, and the number of antral follicles seen on ultrasound...

Risk from Fertility Medications

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In some cases, ovarian stimulation can result in a condition known as OHSS, ovarian hyperstimulation syndrome. Symptoms of OHSS include excessive swelling of the ovaries and buildup of fluid in the body, which can occur in mild to severe forms

depending on your age, clinical situation, and the medications used. The HCG trigger injection can lead to the early onset of OHSS 1 to 5 days after egg retrieval. . . The mild form of OHSS occurs in 5 to 10% of ovarian stimulation cycles. People with this condition will experience moderate abdominal bloating and discomfort that will resolve without medical treatment over the course of 3 to 7 days. Because there is no embryo transfer, more severe forms of OHSS occur in less than .5% of egg freezing cycles. Fluids, may accumulate in the abdomen and pleural space around the lungs, resulting in pain, discomfort, and shortness of breath. This fluid build-up also results in thickening and concentration of the blood, which can raise the risk of kidney failure and blood clots, most commonly in the lungs and legs. These extreme complications occur very rarely, in only 0.2% of all treatment cycles. Severe OHSS typically resolves over the course of 1 to 2 weeks and is effectively treated by administering intravenous fluids, and draining the accumulated fluid. . . . Advancements in fertility research and technology have helped develop strategies that have dramatically reduced the frequency and severity of OHSS. OHSS occurs much less frequently with Egg Freezing cycles and it is typically more mild when it does occur, and it can be managed effectively by diagnosing it early and treating it actively. It's also important to be aware of the controversy surrounding cancer risks that may be presented by injections of FSH.. In the 1990s, a few studies suggested that fertility drugs could result in an increased risk of breast, ovarian, or uterine cancer. Many later studies did not confirm this finding and recognized that the original studies didn't account for the fact that infertility itself is associated with an increased risk of cancer. Millions of people have gone through fertility treatment since these initial studies and there does not seem to be any increased risk of cancer due to fertility drugs. It's important that you carefully consider these studies in making your decision to undergo an Egg Freezing Cycle. Each risk, however small, should be evaluated thoroughly and all questions discussed with your medical team....

Egg Retrieval

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If controlled ovarian stimulation has been completed successfully, the follicles have reached optimum size, and the trigger injection has been administered, the eggs should be ready to be retrieved. The objective is to retrieve mature eggs that can be successfully used in fertility treatment. Your clinical team will provide you with an estimated date for the procedure; however, the timing of egg retrieval is based on your response to the stimulating medications, which will be different for different people. So you should be prepared for your egg retrieval to take place any day of the week, including on a weekend. Your clinical team will let you know when to arrive for the procedure as well as when to refrain from eating and drinking. Egg retrieval is a minor surgical procedure performed under anesthesia that lasts approximately 10 to 30 minutes. Your medical team will retrieve the eggs using an ultrasound probe and needle. With internal ultrasound guidance, the needle is inserted through the upper vaginal wall and into each follicle. Fluid from the follicles is removed through gentle suction that draws it into a tube. As seen on the ultrasound, once the needle has been inserted into the follicle, the fluid, is removed through gentle suction that draws it into a tube.

. An embryologist will immediately examine the fluid for eggs under a microscope. A single egg is present in roughly 65 to 90% of optimal follicles.

In rare cases, no eggs will be retrieved, or none of the retrieved eggs will be of proper maturity to fertilize. This is more likely when very few follicles are present.. Egg retrieval may be postponed if it's suspected that there has been a failure in the delivery or response to the trigger shot, which can happen in 1 to 2% of cycles. If this occurs, it may be necessary to give the shot again and retry egg retrieval two days later. After the egg retrieval procedure is completed, the recovery period begins. Depending on the type of anesthesia that is administered during the procedure, you may experience grogginess, but this will gradually wear off throughout the day. Your medical team may monitor vital signs, such as blood pressure, heart rate, and oxygen saturation. Some cramping may occur after egg retrieval and you may be given pain and/or anti-nausea medications as needed. Once alert and awake, discharge instructions and next steps will be reviewed with you.. Most people leave the recovery room about one hour after the procedure.. The day following the egg retrieval someone from the medical team will call to review your final frozen egg quantity and to see how you are feeling..

Egg Retrieval: The Risks

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While egg retrieval is a routine part of fertility treatment, it is still a minor surgical procedure, which means that there is always some possibility of complications. If IV sedation is used, it may also carry some very rare risks, such as low blood pressure, nausea or vomiting, and in fewer than 1 in every 100,000, cases; death. Because the ovaries are covered with very small blood vessels, there is a chance that the egg retrieval could result in some bleeding. While this bleeding is usually minor and stops on its own, in fewer than 1 in 1,000 retrievals, the bleeding will continue and accumulate in the pelvic and abdominal cavity. If this happens, hospitalization may be required to monitor and manage the blood loss and may necessitate a blood transfusion. In extremely rare situations, people may require surgery to stop the bleeding which could result in the removal of the ovary. In fewer than 1 in 5000 cycles, the enlarged ovary may twist around its blood supply in a complication known as ovarian torsion. This condition cuts off the blood supply to the ovary and can cause severe pain. Surgery may be required to untwist the ovary. Rarely, torsion may result in loss of viability, necessitating removal of the ovary. Less than 1 in 1000 egg retrievals may result in pelvic or ovarian infection. This is more likely if there is severe endometriosis. Endometriosis is a condition in which tissue similar to the uterine lining grows outside the uterus. This can produce a fluid-filled structure in the ovary called an endometrioma. These endometriomas may be punctured in the process of egg retrieval and can become infected. You may be given antibiotics before or after egg retrieval to prevent or treat an infection. Severe infections may require surgery to remove the infected tissue. While unlikely, infections can reduce chances of getting pregnant in the future.. In a very small number of egg retrievals, there can be damage to other organs in the pelvis, including the bladder, ureters, intestines, or major blood vessels.. It's important to be aware of the potential risks associated with Egg Retrieval. Your medical team will take every measure possible to minimize the likelihood of these risks and have established procedures to manage the impact if they do occur.

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Cryopreservation of Eggs

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Cryopreservation of eggs. Once your matured eggs have been retrieved, they will be frozen for long term storage. The most frequently used cryopreservation technology utilizes rapid freezing known as vitrification, in which Eggs are processed with an increasingly stronger solution of cryoprotectants before plunging the eggs directly into liquid nitrogen.. Fertility clinics have caretaker responsibility to both store and maintain cryopreserved eggs. . . . It's important for you to maintain contact with your facility for the duration of time your eggs are frozen, and in most cases, the patient is responsible for paying storage fees. Decisions on discontinuing the storage of frozen eggs may pose challenging, ethical and logistical issues, which you should consider carefully. . The options include allowing one person to use the eggs independently, donating them for use by a third party, donating them for research, or disposing of the eggs . The cryopreservation of Eggs has been safely performed since 2012 the late 1990s. There have not been any indications that children born from frozen eggs are at any greater risk for birth anomalies than children born from IVF with Fresh Eggs fresh egg transfers. .

Laboratory Risks

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Fertility treatment and the storage of sperm, eggs, and embryos involve very complex processes requiring the use of sophisticated equipment by highly trained embryologists. These processes depend on the reliable function of equipment and human consistency. In very rare cases, equipment can fail and even the most highly skilled embryologists can make human errors leading to the loss or compromise of sperm, eggs, or embryos. Very infrequently, damage can occur due to a laboratory accident such as a broken pipette or a dropped petri dish. In extreme cases, the laboratory is vulnerable to natural disasters such as fires, floods or earthquakes, which could damage or destroy the embryology laboratory and everything in it. There are, however, safeguards built into the system, such as backup generators to minimize the risk from loss of power. The most critical and basic responsibility of the embryology laboratory is to be 100% certain that the correct sperm, eggs, and embryos are used for the correct people and procedures. You can rest assured knowing that there are very rigid protocols used for patient identification at every step of the cycle.

Using Your Frozen Eggs

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Using Your Frozen Eggs. When you are ready to use your cryopreserved eggs, they will be thawed in the laboratory. . . . It's important to understand that not all eggs will survive the thaw, and those that do, may not fertilize or develop appropriately. Typically, an egg will be retrieved from 65-85% of follicles over 13mm in diameter.. 60-90% of the eggs retrieved will be mature. If frozen, approximately 85% of mature eggs will survive the thaw and 60-80% of those will fertilize successfully. The eggs will be fertilized using a procedure called intracytoplasmic sperm injection, or ICSI, in which a single sperm is injected into the egg. At this time, medication may be used to support your uterine lining as the fertilized egg develops. These processes are equivalent to the second half of an IVF cycle. Depending on your age when freezing your eggs, about 60-80% of these fertilized eggs will form good-quality embryos by day 3. By day 5 or 6, 20-60% of these day 3 embryos should progress to the most advanced, blastocyst stage. Let's walk through a typical scenario to better demonstrate the decreasing number of embryos. For example, if 15 follicles develop, retrieval may yield 12 eggs, 10 of which are mature. Of those 10 mature eggs, 9 will survive the thaw, 7 are likely to fertilize successfully, 5 may develop into good-quality embryos, and ultimately, 2 blastocysts result. Of course these numbers will vary significantly on a case-by-case basis. These rates are typical, however it should be noted that in some cases, no eggs retrieved will fertilize successfully or develop properly. It's also possible that even if they do develop properly, no embryos will reach the final stage of development and be suitable for transfer or freezing. This is highly dependent on the number of eggs retrieved and the age of the person they were retrieved from. . Using eggs frozen at a younger age result in a higher pregnancy rate than using fresh eggs.

Pregnancy rates decrease over time

so we set a goal to freeze more eggs as people age.

. In people under the age of 35, about 5% of retrievals will yield no embryos to transfer. In people over the age of 42, this rate increases to 40% of retrievals. It's important to remember that this decrease in the number of embryos is expected and you should not be discouraged by it. The processes used by the embryology team are designed to optimize the development of embryos that are most likely to result in pregnancy.

Conclusion

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By now, you should feel informed about the many different processes, procedures, and considerations of freezing your eggs. The challenges posed by Egg freezing can be intimidating, but it can be reassuring to remember it has been practiced for over 10 years and allowed many people to preserve their fertility and plan their families. Continuous improvements and research have led to better pregnancy rates, fewer complications, and easier cycles. Now that you have completed the module, we hope you feel empowered to discuss any questions or concerns with your medical team......