Mount Sinai Fertility
Sinai Health System

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IN VITRO FERTILIZATION (IVF) INFORMATION PACKAGE

Form # MSF-101 (Oct 2016)

Welcome to the Mount Sinai Fertility (MSF) In Vitro Fertilization (IVF) Program. This package contains information about IVF that you are required to read before completing and signing your IVF Consents. In addition, you must review the MSF electronic IVF Video. The video is designed to help you understand the IVF process and procedures.

If you have further questions about the IVF process, please speak to your nurse or book an appointment with your doctor to discuss the IVF cycle.

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PATIENT CHECKLIST FOR IVF

Before you are ready to begin an IVF cycle, the following steps must be taken. Please check with your doctor or nurse if you are unsure which investigations may be required in your situation.

- ☐ Read this information package
- ☐ View the MSF electronic IVF video
- ☐ Blood tests on person undergoing IVF (results take 2-3 wks)
- ☐ Blood tests on partner of person undergoing IVF (if applicable) (results take 2-3 wks)
- ☐ Sperm Wash Assessment (if required)
- ☐ Frozen sperm sample for back-up (if required)
- ☐ Uterus Test: Hysteroscopy or Sonohysterogram
- ☐ Other investigations ordered by your doctor:

  _____ _____

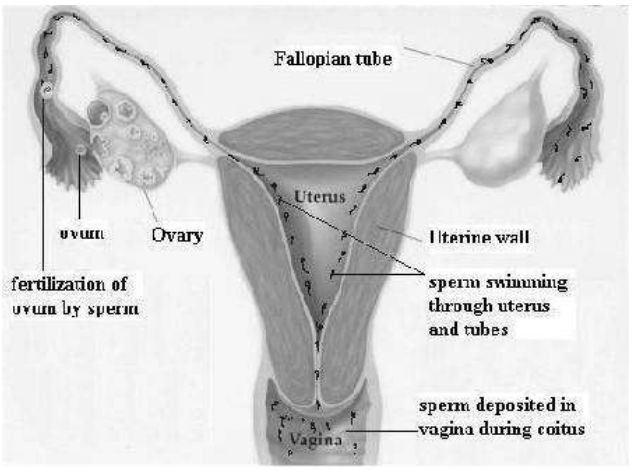
- ☐ Consent package - Consents must be witnessed by a third party. If you have questions about the consent forms, or if you require a third party witness, please book an appointment with a nurse.
- ☐ Call to check if results have been received or if you have questions about IVF in general or your specific treatment. **Call 416-586-4748, option 1.** A nurse will review your chart and inform you if any further steps are needed.
- ☐ If you would like to discuss IVF further before you start your treatment, pleas book an appointment with your doctor.

Once the above steps are completed, you are ready to start your IVF cycle.

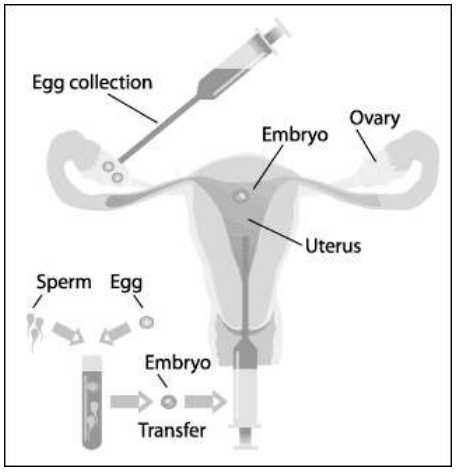
- ☐ **To start your IVF cycle**, patients who have a regular menstrual cycle on their own are to call the **clinic** on the first day of a period (first day of bleeding = day 1). Call **416-586-4748, option 1.** State and spell your name, and that is your day 1 and you would like to start your IVF cycle**.** A registered nurse (RN) will call you back by the end of the next day.
- ☐ At the start of your IVF cycle, call your **Doctor's office** to book a review appointment (if not already booked) to review the completed IVF cycle.

IN-VITRO FERTILIZATION (IVF)

Reproduction inside the body (in vivo) occurs when an egg joins with sperm in the fallopian tube to form an embryo. The embryo then attaches to the uterus (womb) for pregnancy. In IVF, eggs are removed from the body, and eggs and sperm are joined in the laboratory to form embryos. These embryos are then placed into the uterus for pregnancy.



In vivo reproduction

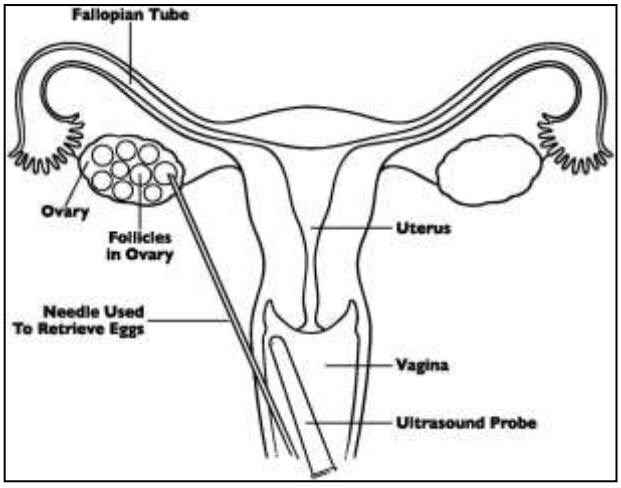


In vitro fertilization

IVF treatment usually requires stimulation of the ovaries to produce multiple eggs using fertility medications, an egg retrieval procedure to remove eggs from the ovaries, fertilization (joining) of eggs and sperm in the laboratory to form embryos, growth and assessment of embryos for 3 to 5 days and finally the placement of embryo(s) into the uterus to achieve a pregnancy.

Ovarian Stimulation:
In a typical menstrual cycle, only one mature egg is produced each month. To increase the chances of success in IVF, hormonal medications are given to stimulate the ovaries to produce and grow more eggs, which can be removed for the IVF process. Fertility medications are injections which must be given daily for approximately 2 weeks. You will also be given an injection medication to prevent your natural ovulation. During this time period, frequent blood tests and internal ultrasounds are required in order to monitor the effects of the medications.

Egg Retrieval:
The egg retrieval is performed by a doctor. The doctor will use an ultrasound to see the follicles and place a needle through the top of the vagina into the ovary. All of the follicles will be drained, and the fluid will be sent to the embryology lab to identify the eggs. Shortly after the retrieval you will be told the number of eggs that were retrieved.



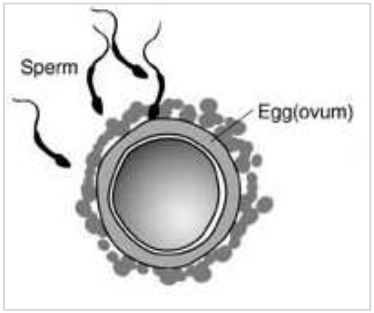
The egg retrieval will be performed with sedation. Medications to relax you and provide pain relief will be given through an intravenous (IV) during the procedure. You will not be completely unconscious, but should be comfortable and able to tolerate the procedure.

Sperm Sample:
A sperm sample is required on the day of the egg retrieval. Depending on your circumstance, this may be obtained by either:

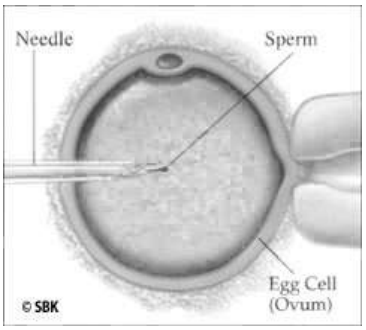
- Fresh ejaculate
- Frozen sperm sample
- Donor sperm sample
- Sperm retrieval procedure performed by a urologist (for those without ejaculated sperm)

If a fresh sperm sample is planned, to avoid any issues with sample production on the day of egg retrieval, a back-up sample can be frozen ahead of time. Please inform a doctor or nurse if a back-up sample is preferred.

Fertilization:
After the egg retrieval, the embryology lab will fertilize the eggs by IVF or Intracytoplasmic sperm injection (ICSI). Fertilization is the process where the egg and sperm join together to form an embryo. Typically, it is expected that approximately 70-80% of mature eggs should fertilize. Your doctor will discuss which option for fertilization would be best in your situation based on your history and test results.



IVF is a process where a small sample of sperm is placed with each egg to allow the sperm to naturally fertilize the egg.

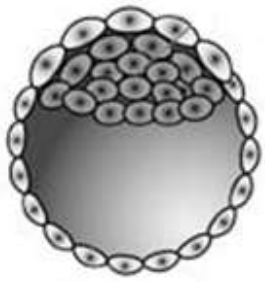


ICSI is a procedure in which a sperm is chosen and mechanically placed into an egg for fertilization. ICSI is used when sperm counts are low, sperm quality is poor, previous failed fertilization with IVF, unexplained infertility, pre-implantation genetic diagnosis (PGD) or when there are other concerns about fertilization.

Embryo Development and Assessment:
Embryos will be placed in an incubator and checked by the embryology team. You will receive a regular report about the number of embryos which are growing.

Over the first few days, embryos will start to grow and divide. By the 3rd day, they should be between 6-10 cells. By the 5-6th day, they should have developed into a blastocyst and will contain hundreds of cells and a fluid cavity.

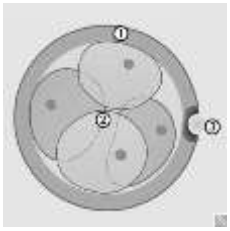
Day 3 Embryo



Day 5/6 Blastocyst

Blastocyst culture means that the embryos will be grown from day 3 to day 5 in the laboratory. We only expect half of all embryos to survive during this time. Blastocyst culture allows us to pick the best embryos by picking the ones that are growing the best on day 5.

Laser Assisted Hatching:

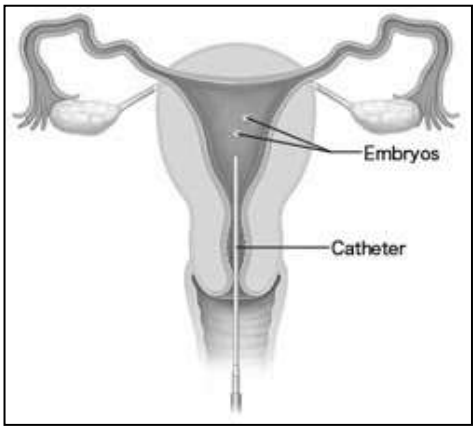


Each embryo is surrounded by a shell called the zona pellucida. The embryo at the blastocyst stage must hatch out of the shell in order to implant into the uterus. It is felt that in some situations, the embryo may not be able to properly hatch out of this shell to implant. Assisted Hatching is a laboratory procedure where a laser is used to thin or make a small hole in the shell around the embryo to make it easier for the embryo to hatch.

Assisted hatching may benefit those whose embryos were created with eggs retrieved after the age of 37, those with poor quality embryos, those with previous repeated IVF implantation failures, and frozen embryos. Assisted hatching may not benefit all individuals undergoing IVF treatment.

There is a theoretical risk of damaging the embryo with assisted hatching; however this has not happened in our experience due to the precision of the laser. Some studies have suggested there is an increased risk of identical (monozygotic) twins after assisted hatching.

Embryo Transfer:



The embryo transfer will occur either on day 3 or day 5 after the egg retrieval. You will have a discussion with the doctor and embryology team about your embryos. A final decision will be made about the number of embryos which will be transferred, based on age, medical history and the number and quality of the embryos.

As people get older, more eggs and embryos may be abnormal. Therefore, more embryos may be transferred in those in their late 30s and 40s. In younger individuals <35, usually only 1 or 2 embryos will be transferred. Preimplantation genetic screening (PGS) which is also known as comprehensive chromosome screening (CCS) is a technology that can be used to test embryos for abnormalities. PGS/CCS results in more information about the embryos and can allow for fewer embryos to be transferred.

The embryo transfer is performed by a doctor. An ultrasound is used to see the uterus, and the embryos are placed in the uterus using a small catheter (tube) through the cervix.

Pregnancy Test:

You will be instructed when a pregnancy test to see if the IVF was successful should be done. If the pregnancy test is positive, it will need to be repeated no sooner than 2 days later to confirm the pregnancy is growing appropriately.

A vaginal medication (progesterone, prometrium, endometrin, crinone) is started after the egg retrieval to help the uterus prepare for implantation. The medication should be taken until the pregnancy test is done and will be continued if pregnancy is confirmed.

EMBRYO FREEZING

Sometimes more embryos are produced than will be transferred during a fresh IVF cycle. Occasionally, for various medical reasons, it will be advised not to proceed with a fresh embryo transfer and to freeze all of the embryos. Embryos that are good quality can be frozen (cryopreserved) until you are ready to use them in the future. Frozen embryos avoid the need to repeat the entire IVF cycle. Embryos can be frozen for long time periods and still have a good chance to lead to pregnancy. Embryos must be of good quality and have developed to certain stages before they can be frozen. About 25% of patients will have extra embryos that can be frozen.

Embryo cryopreservation involves several steps to allow the embryo to be frozen. Embryos are dehydrated with cryoprotectants, cooled and placed into straws and stored in liquid nitrogen. Embryos are labeled with your information and double checks are done at each stage to prevent mix-ups.

There is an 80-90% chance an embryo will survive the freezing and thawing process. This will not be known until the lab thaws the embryos for your frozen embryo transfer. Frozen embryos have a slightly lower chance of success.

A frozen embryo cycle involves preparing the uterus for implantation. This may involve medications and/or monitoring by ultrasound to determine the appropriate timing to transfer the embryo(s). The embryo(s) will only be thawed when it is determined that the uterus is ready for embryo transfer. The embryo transfer usually occurs about 2 weeks into the menstrual cycle.

Studies have not shown any increased risk of birth defects with embryo freezing.

Your doctor will discuss if other investigations are needed before the frozen embryo transfer. In addition, you will discuss the number of embryos which will be thawed each time.

MOUNT SINAI FERTILITY EMBRYO DONATION PROGAM

Mount Sinai Fertility has developed an embryo donation program to help people who are unable to form their own healthy embryos. Those who have frozen embryos that they will not use themselves can choose to donate the embryos. The embryo donation program is monitored by a special advisory group comprised of doctors, nurses, embryologists, a social worker and a bioethicist.

RESEARCH AND TRAINING

Research is important to continue to improve the success of IVF. During an IVF cycle, you may have excess eggs, sperm, follicular fluid, granulosa cells or embryos that cannot be used to establish a pregnancy, but may be used for research and training. We encourage the donation of excess biologic material to help aid in improving IVF in the future. All research studies at Mount Sinai Fertility have been reviewed and approved by the Mount Sinai Hospital Research Ethics Board.

OUTCOMES

Mount Sinai Fertility tracks the outcomes of all IVF treatment cycles, including information about pregnancies and births. This information helps us to continue to improve our treatments and patient care. You may be contacted in the future and asked to provide information regarding pregnancy and outcomes.

IVF OUTCOMES AND RISKS

MEDICATION RISKS

Most people will experience some bloating and fullness in the lower abdomen with the IVF cycles. This is a normal reaction to the medications and often indicates the medications are stimulating egg development. Side effects of the medications may include bruising and soreness at the injection site, allergic reaction, gastrointestinal distress, headaches or mood changes. It is important to discuss with your doctor if you experience any reactions to the medications.

Currently there is no definite evidence directly linking fertility medications to breast or ovarian cancer, although there may be an increased risk of borderline ovarian tumours. Those with infertility, regardless of exposure to fertility medications, have a higher risk for ovarian cancer. However, further long-term studies are needed to determine if there is an association between fertility treatments and breast or ovarian cancer.

OVARIAN HYPERSTIMULATION

Ovarian hyperstimulation syndrome (OHSS) is a condition where there is an over-response to medications with the development of a large number of follicles and very high hormone (estrogen) levels. In severe cases, people will have fluid (water) build up in their abdomen and lungs and develop blood clots. The fluid may need to be removed with a needle and there may be a need to be admitted to the hospital for management. Severe OHSS can occur in 1-3% of people undergoing IVF. Rarely, an ovary that has been stimulated may twist (ovarian torsion), which may require surgery (<1%).

PROCEDURE RISKS

Risks associated with the egg retrieval include: discomfort during the procedure, bleeding, infection or puncture of bowel. Infections are rare, but severe infections may require antibiotics or rarely surgery. The risks of sedation include being too sedated, breathing and/or heart rate complications.

CYCLE CANCELLATION

In some situations, your IVF cycle may be cancelled before the egg retrieval. Approximately 10% of IVF cycles may be cancelled. Reasons for cancelling an IVF cycle may include:

- The ovaries are not responding to medications (too few follicles developing)
- An unusual response to medications (follicles developing too quickly or too slowly)
- Hormone levels too high or too low
- Findings on ultrasounds or blood tests that would decrease the chance of pregnancy
- Ovarian hyperstimulation

When there are a low number of follicles developing, there is a very low chance of pregnancy. Because of the risks and costs associated with an egg retrieval and IVF procedure, a doctor may advise cancelling the cycle if it is felt the chances of pregnancy are small.

If your cycle is cancelled, a review appointment will be booked with your primary doctor and a portion of your costs will be refunded based on the treatments/procedures which have already occurred.

In some cases, and if applicable, it may be possible to perform an insemination when the IVF treatment has been cancelled. The chances of pregnancy with insemination are lower than an IVF treatment, but the treatment is less invasive and less costly.

MULTIPLE PREGNANCY

The goal of IVF is to produce **one healthy baby**.

Multiple pregnancies are pregnancies with more than one baby (such as twins or triplets). This risk of having a multiple pregnancy is increased with IVF, especially when more than one embryo is placed in the uterus. Approximately 1 out of every 5 pregnancies after IVF is a multiple pregnancy. For those under 35 years of age, this risk can be much higher in some situations, and your doctor may recommend only placing ONE embryo during your treatment.

Even twin pregnancies can have many risks to the person carrying the pregnancy as well as to the babies. Risks with multiple pregnancies include miscarriages, premature delivery, or long-term health and developmental problems such as cerebral palsy. The table* below outlines some risks with multiples versus one baby (singleton).

	SINGLETON	***TWINS***	***TRIPLETS***
BIRTH WEIGHT	3,300 grams (7.3 lbs)	2,300 grams (5.1 lbs)	1,660 grams (3.7 lbs)
DELIVERY (FULL TERM = 40 WKS)	38.6 weeks	35 weeks	32 weeks
NEONATAL INTENSIVE CARE UNIT (NICU) ADMISSION LIKELIHOOD	1-2%	25%	75%
NICU LENGTH OF STAY		20 d	30 d
% MAJOR LONG-TERM HANDICAP			20%
RISK OF CEREBRAL PALSY		4x higher	17x higher
RISK OF DEATH IN FIRST YEAR OF LIFE		7x higher	20x higher

There are also increased risks to an individual carrying a multiple pregnancy. This includes higher risks of high blood pressure and diabetes. You may also require bed rest or time off work much earlier. There is also an increased risk of problems with bleeding and problems at the time of delivery.

Parents of multiples also face psychological, social and economic challenges unique to multiple pregnancies. Parenting multiples is more physically challenging and parents often require help. The costs of raising multiples is often more as car seats, high chairs, etc must be purchased in multiple quantities. In addition, there may be additional financial costs if there are long-term health problems.

If you are pregnant with a multiple pregnancy, you should discuss your options with your doctor. In some cases, a pregnancy naturally reduces the number of fetuses early in the pregnancy. In other cases, you may discuss the option of a selective reduction. This is a procedure performed around 3 months by a specialist to reduce the number of fetuses in a multiple pregnancy. This can be a difficult decision to make and a referral to a high-risk pregnancy clinic to discuss this option with a specialized team would be made.

** Information adapted from: One at a Time, UK "One at a Time: The journey towards single embryo transfer" and ASRM Patient Information: "Multiple Pregnancy and Birth: Twins, Triplets, and High-order Multiples. A Guide for Patients" and "Challenges of Parenting Multiples".*

PREGNANCY RISKS

All pregnancies have a small risk that the babies can have a birth defect. The general risk for all pregnancies is approximately 3-5%. The risk of birth defects including cerebral palsy appears to be higher in those with infertility, even if they conceive without fertility treatment. The risk in babies born after IVF appears to be slightly increased (7%), but not statistically different from those with infertility who conceive without the use of fertility treatments. The risk is slightly higher after ICSI (10%). Certain rare conditions have been associated with IVF (Beckwith-Wiedemann syndrome and Angelman syndrome), although they still occur in less than 1% of babies born after IVF or IVF/ICSI. This is an issue which continues to be studied.

Other problems which can occur in pregnancy may also occur in an IVF pregnancy. In particular, miscarriages (spontaneous abortions) occur in approximately 15%-30% of IVF pregnancies (depending on age) and ectopic pregnancies (pregnancy in the fallopian tube) will occur in about 2% of IVF pregnancies.

Studies have also shown that pregnancies conceived through IVF are more likely to have some pregnancy complications including high blood pressure, premature delivery, operative delivery, and small babies. There is no evidence that children born from IVF have neurological or health effects, although further long-term studies are needed.

SPECIAL CIRCUMSTANCES

EGG DONORS / GESTATIONAL CARRIERS

Egg donation is a treatment for individuals who are unable to produce good quality eggs themselves. Egg donation must be by a known or anonymous altruistic donor. Altruistic means that the donor cannot receive any form of compensation for donating their eggs and services, and can only be reimbursed for receiptable expenses.

A gestational carrier, also known as a gestational surrogate, may be required for those who are unable to safely carry a pregnancy. A gestational carrier is a person who undergoes an embryo transfer in order to achieve and carry a pregnancy for another person/couple, who will be the intended parent(s) of the child. The gestational carrier is not genetically linked to the child.

Mount Sinai Fertility does not recruit egg donors or gestational carriers; therefore, an intended parent/parents must find their own donor or carrier. All parties must have independent legal and psychological counseling as well as a medical assessment prior to treatment.

PREIMPLANTATION GENETIC DIAGNOSIS/ SCREENING (PGD/ PGS)

Preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS) are genetic tests performed on cells removed from embryos created through IVF. PGD helps detect genetic diseases while PGS (also known as comprehensive chromosome screening or CCS) screens for abnormal chromosome numbers (aneuploidy). Ideally, after PGD/PGS, genetically normal embryos are selected for transfer.

Aneuploidy refers to the presence of an abnormal number of chromosomes in a cell, for example a human cell having 45 or 47 chromosomes instead of the usual 46. On the contrary, a *euploid* embryo has the normal number of chromosomes which, in humans, is 46. Sometimes PGS detects what is known as *mosaicism* which describes a situation in which different cells in the same embryo have different numbers or arrangements of chromosomes. When people only have mosaic embryos available for transfer, genetic counselling is advised prior to embryo transfer.

FERTILITY PRESERVATION

Some patients, who have not yet had the chance to start or complete their family, require treatment or medication that can cause impairment or loss of fertility. For example, a person who will be undergoing cancer treatment, a transgender person who will be starting hormone treatment, or a person having their ovaries surgically removed. As a result, many patients want to consider the option of preserving their fertility through gamete (egg or sperm) or embryo freezing before starting treatment.

To preserve the full range of options, fertility issues should be discussed as early as possible when planning any sort of potentially fertility-compromising treatment. If you are already receiving or have received fertility-compromising treatment, it may still be possible to pursue fertility preservation but each situation needs to be assessed individually. Please have your care provider send us a referral so we can discuss these options with you.

At Mount Sinai Fertility, when required, we expedite referrals for sperm banking and for those wanting to receive a medical consultation to discuss their medical and cancer-associated fertility risks.

EGG FREEZING

MSF has been freezing eggs as a method of fertility preservation before cancer treatment for many years. We use the process of vitrification, or 'fast freeze' of eggs, which is currently thought to offer the best chance of eggs surviving the freeze/thaw procedure intact.

To date, more than 5,000 babies have been born from frozen egg cycles around the world. Mount Sinai Fertility, as is true for most clinics, currently does not have much clinic-specific data on freeze/thaw survival of frozen eggs and ongoing pregnancy rates resulting from embryos created with frozen eggs. This is because, few patients who have frozen eggs with our programme have yet come back to use them.

The option of freezing eggs has expanded beyond people hoping to preserve their fertility before cancer treatment. In fact, people are choosing to freeze eggs for several reasons including:

- A family history of infertility or early menopause
- A history of endometriosis
- Before ovarian surgery
- Before beginning medication that may impair fertility
- A wish to delay having a family for career or personal reasons such as financial stability or a lack of a partner

For those who are delaying having children until later in life in order to find a good partner, establish a career, become financially secure or other reasons, the negative impact of age on fertility can be significant. Specifically, age negatively impacts the supply of eggs, with both quality and quantity rapidly declining after age 35. Elective egg freezing, also known as elective oocyte cryopreservation (EOC) or oocyte banking for anticipated gamete exhaustion (AGE) allows someone an option to freeze eggs to be used later in life when ready to start a family.

Before starting treatment, you will meet with one of our doctors or Nurse Practitioner for a consultation. We will discuss your goals for egg freezing, the procedure, and advise you on your likelihood of successfully becoming pregnant in the future from frozen-thawed eggs. You will require a transvaginal pelvic ultrasound and bloodwork to test your ovarian function or reserve and screening bloodwork for infectious diseases. You will be given an electronic link to a slide presentation to watch about the process of ovarian stimulation for egg freezing and will have the option of having Psychosocial Counselling.