OOCYTE (EGG) FREEZING

AART offers oocyte cryopreservation, also known as “egg freezing” for patients who are about to undergo treatment for cancer or gender affirmation and choose to freeze their eggs in advance of treatment.

AART also offers egg freezing for age-related fertility decline (often referred to as “elective egg freezing”), for patients who choose to store their frozen eggs for non-medical purposes. The intention of the procedure is that the patient may later choose to have the eggs thawed, fertilized, and transferred to the uterus as embryos, to facilitate a pregnancy in the future. Ovaries age more rapidly than other organs and tissues. As a result, fertility declines at an increasing rate after age 35. For this reason, some patients consider freezing their eggs if they expect a delay in starting a family, in order to provide more options in the future if spontaneous conception is not possible.

CHECKLIST FOR EGG FREEZING

To undergo Egg Freezing at AART, there is a checklist of testing and other clinic items that must be completed prior to beginning. Unless otherwise stated, testing is valid for 1 year.

- Up to date pap test (3 years unless you have had an abnormal pap in the past)
- Swabs for chlamydia and gonorrhea
- FSH, TSH, Estradiol blood tests
- Infectious disease blood tests (rubella, HepB, HepC, HIV, syphilis)
- Blood type
- BMI less than 40
- AFC

Prior to beginning, you must complete a consent package. You will also have to pay for your cycle in full prior to beginning. It is recommended to contact us a month prior to beginning to ensure all of your checklist items are complete and on file.

POLICIES

To undergo ovarian stimulation at AART, you must be under the age of 44. The American Socierty of Reproductive Medicine has deemed ovarian stimulation over the age of 44 as futile treatment as there is a less than 1% chance of a live birth. As a result of this, AARTs age limit is under 44 years of age.
If patients have frozen embryos and wishes to use them after the age of 44, AART can perform a Frozen Embryo Transfer up to the age of 51.

AART does not operate in a hospital setting. The Department of Anesthesia does not recommend out of hospital anesthesia be given in patients with morbid obesity. Additionally, patients with morbid obesity have an increased risk of being poor responders to stimulation and can be difficult to scan (ultrasound). For these reasons, if a patient has a BMI greater than or equal to 40, they will not be offered an ovarian stimulation cycle at AART. If patients can reduce their BMI to below 40, they can proceed with treatment.

All cycle fees must be prepaid. If a cycle is cancelled there will be a refund for services not yet completed. Medication fees are separate and non-refundable.

BLOODWORK

Your physician will likely order blood tests as part of your initial workup. AART requires infectious disease screening for all patients who are planning treatment with us. Bloodwork ordered for the individual providing the eggs (oocytes) will have timed hormonal bloodwork ordered. Bloodwork ordered for all patients and their partners will include Hepatitis B, Hepatitis C, HIV and syphilis. Currently to have bloodwork completed in the Maritime provinces, you will have to book an appointment at a location closest to you. There are exceptions to this and some clinics offer walk-in appointments.

Nova Scotia has an online booking portal found here: https://booking.nshealth.ca/

New Brunswick residents can call ahead to book, some locations have walk-in service.

Prince Edward Island residents must call the site to prebook an appointment.

Once bloodwork has been drawn, it can take up to two weeks for AART to receive the results.

ANTRAL FOLLICLE COUNT

As part of the testing for an egg freezing cycle you will be required to have an ultrasound to count your follicles. This is called an antral follicle count or AFC, which is completed using a vaginal ultrasound. To book this test, contact the nurses when you get your day 1 of your period and they will schedule the ultrasound for you. This test is usually completed between day 2-5 of your cycle.

MY TESTING IS DONE, NOW WHAT?

Once you have all of your testing completed and/or scheduled, please reach out to our administration staff to book in for a follow-up appointment to review the results with your physician. At this appointment, you can discuss the best treatment options based on your results.

EGG FREEZING TREATMENT CYCLE

During each menstrual cycle, the ovary releases one egg (oocyte). In egg freezing, medication is given in order to encourage a larger number of mature eggs. Eggs develop in small fluid spaces (follicles) within the ovary. As follicles grow, the hormone **estradiol** is produced. When estradiol reaches a certain level and the follicles reach an appropriate size, another hormone, luteinizing hormone (LH) is released which is the driving force that is necessary for final maturation and release of the egg. This process is known as **ovulation**. During the treatment, human chorionic gonadotropin (HCG) is given as an injection which works in a similar way to LH, and the eggs are collected before ovulation can take place.

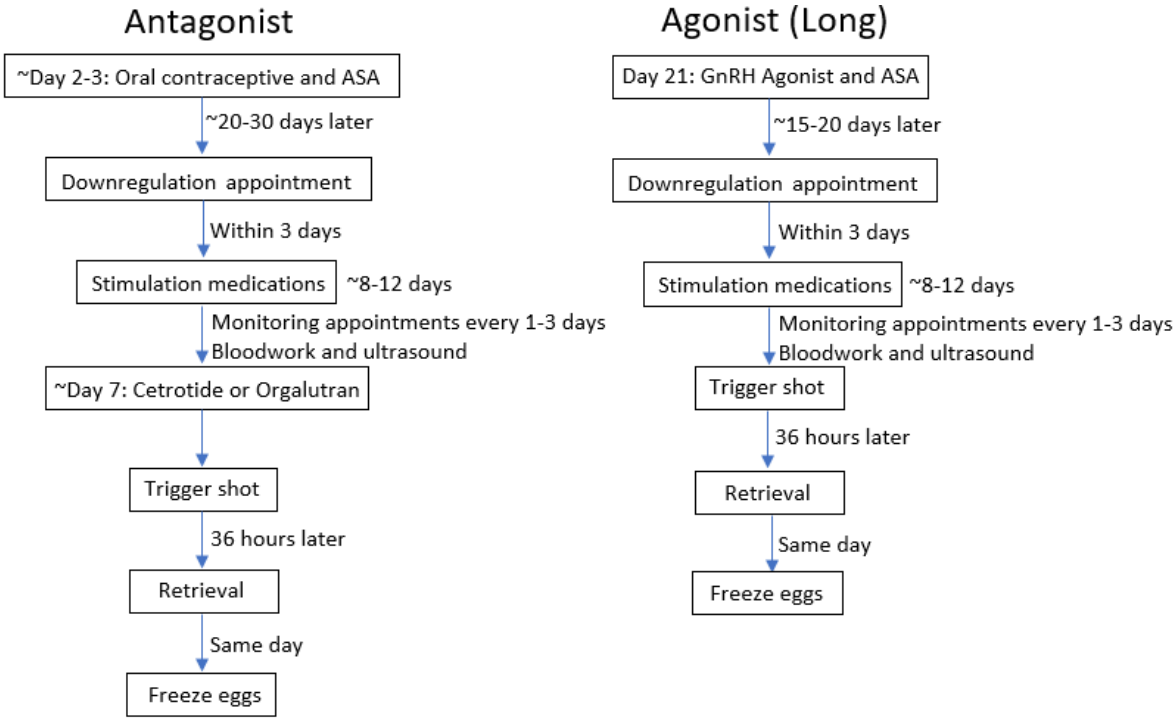
Once the eggs are collected, they are cryopreserved in liquid nitrogen. While they can remain frozen indefinitely, it is recommended that the patient uses them before age 51, which is the natural age of menopause. Patients should consider the risks of pregnancy at advanced maternal age (over 35), including gestational diabetes, preeclampsia, c-section delivery, preterm delivery, and low birth weight when deciding on a timeframe for using their eggs. If the patient is over 51,

or if other health conditions prevent pregnancy when they choose to use their frozen eggs, they can use a gestational carrier. Please see AART's age limit policy for more information.

Patients with frozen samples stored at AART are required to pay the annual storage fee for each year. If storage fees lapse for more than one year the eggs will be disposed. If a patient chooses to dispose of their eggs, a form will be provided.

STEPS IN EGG RETREIVAL AND CRYOPRESERVATION

There are two main protocols used at AART for ovarian stimulation (your physician may recommend another or make modifications to these). Every protocol for cycles at AART begins by alerting our nursing staff when you get your day 1 of your cycle. The two main protocols are outlined below.



a) **Agonist Cycles- GnRH Agonists: *Suprefact (Buserelin Acetate)* or Lupron (*Leuprolide Acetate*):** Administration of Suprefact or Lupron causes suppression of ovarian function by shutting down hormone secretion by the pituitary gland. Suprefact is administered by subcutaneous injection and Lupron is administered intramuscularly. These medications are self-injected. Side effects associated with these medications are uncommon. Occasionally patients experience hot flashes, a decrease in libido (sex drive), or a local reaction at the injection sites.

b) ***Gonadotropins (eg. Gonal-F and Menopur):*** These hormones stimulate the follicles

to grow. Gonal-F is a pure form of FSH (Follicle Stimulating Hormone) which has been synthetically produced. Menopur is a mixture of FSH and LH (Luteinizing Hormone). These are administered by subcutaneous injection. These medicines can be self-injected (you will be taught how to do this). Overstimulation of the ovaries (hyperstimulation) may also occur. If the ovaries become overstimulated, treatment with gonadotropins may have to be stopped and the cycle cancelled or the embryos may be frozen. The embryo(s) are then transferred in a subsequent frozen embryo transfer cycle.

c) **Antagonist Cycles-** ***Cetrotide or Orgalutran:*** This hormone antagonist inhibits early ovulation by suppressing the production of LH or luteinizing hormone. This medication is administered in the morning as a subcutaneous injection. We will tell you when to begin this medication. This injection may cause a local reaction at the injection site.

d) ***Human Chorionic Gonadotropin (HCG) "Trigger Shot"***: HCG is a hormone that acts in the same way as the natural hormone LH. LH normally is produced by the pituitary gland and acts as a final "driving mechanism" to mature the eggs. HCG is given by subcutaneous injection into the abdomen. Following the administration of HCG, retrieval of the mature eggs is performed approximately 36 hours later.

MONITORING OF THE OVARIAN STIMULATION

Your first appointment during your cycle is called a downregulation appointment. At this appointment you will have a blood test and ultrasound to determine if you are ready to begin stimulation medications. At downregulation we want to ensure all of your follicles are small, and there are no active cysts present, and your estrogen and LH levels are low. This will indicate if your follicles that will grow at the same time and speed.
The rest of your monitoring appointments will either be bloodwork only (typically day 5 of stimulation) or both bloodwork and ultrasound.

a) ***Blood Tests***: Blood testing allows team members to follow the growth and development of follicles. These blood tests are done on a first come, first serve basis between 7:30am and 8:15am at AART. You will be informed of the results by the nursing team.
b) ***Ultrasound Examination***: Vaginal ultrasound examinations are performed to monitor follicle development. Ultrasounds are completed after your bloodwork during your appointment.
c) ***Cancellation***: Some patients will have their cycle cancelled (less than 10%). Cancellation may be necessary if the ovaries do not respond to the medications or if they respond too much.

EGG RETRIEVAL

Patients are admitted to AART as outpatients in the morning one hour prior to oocyte retrieval. You must be fasting (nothing to eat or drink) since midnight before. An intravenous infusion (IV)

is started before this procedure and conscious sedation is used. A support person may be present for this procedure. Discomfort is well controlled with intravenous medication. To retrieve mature oocytes (eggs), a vaginal ultrasound probe is used to guide the aspiration needle. Oocytes are removed from the follicles by suction. This technique is known as **follicle aspiration**. On average, 70-80% of follicles contain oocytes. An embryologist examines the fluid under a microscope to identify the eggs (oocytes). After the procedure you will be monitored in the recovery area at AART. Once released, you should rest at home for 24 hours after your procedure.

EGG FREEZING

Vitrification is a process whereby water molecules in the eggs are removed and replaced with a high concentration of cryoprotectant. The eggs are then plunged directly into liquid nitrogen. This rapid freezing creates a glass transition temperature (glass state) and the eggs are cryopreserved (frozen). This quick freezing reduces the chance for intracellular ice crystals to be formed, thus decreasing the degeneration of cells upon warming for fertilization.

RISKS ASSOCIATED WITH EGG FREEZING

- Mild discomfort and bruising of the arm may result from repeated blood testing.
- Vaginal ultrasound-guided egg retrieval is usually associated with some discomfort.
- Conscious sedation is used during the retrieval process, which may cause drowsiness, nausea and low blood pressure. To decrease the risks of conscious sedation, our clinic policy is that patient BMI must be below 40.
- Rarely there can be side effects and complications associated with medications used for sedation which may require medical treatment and/or transfer to hospital by ambulance.
- Trauma to adjacent structures (such as bowel, bladder, blood vessels, and other pelvic structures).
- Rarely, an ovarian tissue rupture may occur. In less than one percent of cases, bleeding or a pelvic infection may also occur after the egg retrieval.
- In rare cases, there may be no oocytes retrieved.

OHSS INFORMATION SHEET

Severe ovarian hyperstimulation syndrome (OHSS) is a potentially serious complication of ovarian stimulation for IVF or egg freezing. OHSS affects 1 in 10 patients who undergo ovarian stimulation. Severe OHSS affects about 1-3% of ovarian stimulation patients.

Fertility drugs stimulate the ovaries to produce many egg sacs (follicles). Sometimes there is an excessive response to fertility drugs and this causes OHSS. Overstimulated ovaries enlarge and release chemicals into the bloodstream that make blood vessels leak fluid into the body. Fluid leaks into your abdomen and, in severe cases, into the space around the heart and lungs. OHSS can affect the kidneys, liver, and lungs. A serious, but rare, complication is a blood clot (thrombosis). A very small number of deaths have been reported worldwide.

SYMPTOMS

The most common symptoms of OHSS are: abdominal swelling or bloating (because of enlarged ovaries or fluid retention), nausea, and, as the condition gets worse, vomiting.

- Mild OHSS - mild abdominal swelling or bloating, abdominal discomfort and nausea. Mild symptoms are common in patients undergoing ovarian stimulation.
- Moderate OHSS – symptoms of mild OHSS but the swelling and bloating is worse because fluid is building up in the abdomen, associated with abdominal pain and vomiting.
- Severe OHSS - symptoms of moderate OHSS plus extreme thirst and dehydration, increased fluid buildup in the abdomen, passing very small amounts of urine which is very dark in color (concentrated), difficulty breathing because of build-up of fluid in the chest and (rarely) a red, hot, swollen and tender leg due to a clot in the leg or lungs (thrombosis).

If you develop any of the symptoms you need to seek medical help immediately by calling our nursing line. If it is outside business hours and you are concerned, please go to the nearest emergency room. Please track your symptoms.

RISK FACTORS

The risk of OHSS is increased in patients who:

- have polycystic ovaries,
- are under 30 years,
- have had OHSS previously,
- get pregnant, particularly if this is a multiple pregnancy (twins or more),
- have very high blood levels of estradiol in response to FSH injections, and/or
- have very high numbers of follicles develop in response to FSH injections.

FUTURE USE OF OOCYTES

While egg freezing may be successful, there is a risk that eggs might not survive the freezing and warming process largely due to egg quality. International studies suggest that the survival rates vary from 80-90% per egg. Only good to excellent quality eggs are vitrified in order to achieve this survival rate.

Eggs could survive the vitrification and warming process, but might be damaged during the process, making them unsuitable for fertilization. Intracytoplasmic sperm injection (ICSI) must be used to inseminate the eggs. International studies suggest the chance of successful fertilization of cryopreserved and warmed eggs using ICSI is 70-80% per egg. Vitrified eggs yield fewer embryos than fresh eggs. Studies show that there is almost double the blastocyst rate with fresh eggs versus frozen eggs.

There is very limited data on live birth rates after egg freezing, but existing data suggests similar clinical pregnancy rates after transfer of embryos obtained by either frozen or fresh eggs. More than one cycle may be required to obtain the number of mature eggs that are desired. The table below provides information on cumulative live birth rate by age of egg provider:

Table 6. Cumulative live birth rate per batch of oocytes retrieved (from CARTR-BORN Jan 1, 2013–Dec 31, 2014, after all resulting embryos, fresh and frozen, have been transferred or discarded)

Number of mature eggs retrieved	Age of oocyte provider				
	Less than 30	30–34	35–37	38–40	41–42
<5 eggs	20.3%	21.3%	17.0%	11.7%	5.9%
5–9 eggs	35.6%	38.3%	31.4%	23.8%	13.4%
10–14 eggs	46.8%	45.3%	41.9%	31.8%	21.8%
15–19 eggs	46.8%	51.1%	45.5%	33.2%	30.3%
20–24 eggs	47.6%	53.1%	50.3%	45.9%	26.7%
25+ eggs	43.7%	48.9%	53.1%	54.0%	40.9%
Total	38.5%	38.3%	30.9%	21.8%	12.5%

The age at which a patient freezes their eggs and the number of eggs that are frozen impact the probability that these eggs will enhance their fertility.

There is a chance that a patient who undergoes egg freezing may not need to use their frozen eggs in the future and there are no guarantees that the frozen eggs will produce a viable pregnancy. Patients are encouraged to consider what they will do with their frozen eggs if they don't use them in the future. The current are options to: donate them to science to help with research and training, dispose of them, or act as a known egg donor to someone you know personally who is struggling with infertility.

WHAT HAPPENS IN THE EVENT OF DEATH?

According to the law, eggs are considered property, so in the event of death they are treated as such. A notarized will is required in order to outline what you want to be done with your eggs in the event of your death. If you do not have a notarized will, eggs will be subject to the *Intestate Succession Act.*