

Preserving Your Fertility

Risks Of Cancer Treatment

The risk of infertility from cancer treatment depends on many things, like your cancer type, age and pre-treatment fertility status. Treatment specifics such as duration and dose of chemotherapy or radiation and location and scope of surgery or radiation also impact fertility. Specifically, treatment can cause the following:

- The ovaries no longer contain a supply of health eggs
- Damage to the reproductive system prevents a fertilized egg from successfully implanting and growing in the uterus
- Damage to the reproductive system prevents you from being able to carry a pregnancy

To understand your risk visit: www.livestrong.org/we-can-help/fertility/risks

Fertility Preservation Options Pre-Treatment

1) Oocyte Cryopreservation (Egg Freezing)

This process involves ovarian stimulation, egg harvesting, egg freezing

- Ovarian Stimulation: you will take a series of daily injections for approximately 9-14 days. During that time you will have vaginal ultrasounds and blood collected every 2-3 days.
- Egg Harvesting: Once we have the maximum number of eggs we can grow you will take one final shot to prepare the eggs for harvest. Egg harvesting is completed by using a vaginal ultrasound with an attached needle to extract the egg from the ovaries. This is completed under sedation ("twilight sleep") and through needle punctures in the vaginal wall. Recovery is typically 24-48 hours.
- Egg freezing is completed by a process called vitrification, which rapidly freezes the eggs. These eggs can then be stored for an unlimited amount of time for future use.
- In the future, eggs can be thawed and injected with male sperm for fertilization, embryos will then be placed in your uterus or a surrogate's uterus to achieve pregnancy.

2) Embryo Cryopreservation

This process involves ovarian stimulation, egg harvesting (see Oocyte cryopreservation for these details), fertilization of eggs with sperm and embryo freezing

- Fertilization of eggs is completed by mixing eggs and sperm together in a petri dish or injected sperm directly into the eggs. You can use your partner's sperm or a sperm donor for this process. This process will be determined by your physician based on testing and sperm quality.
- Embryos will then be frozen by a process called vitrification, which rapidly freezes the embryos. These can then be stored for an unlimited amount of time for future use.
- In the future, embryos will be thawed and then placed into your uterus or a surrogate's uterus to achieve pregnancy.

3) Ovarian Tissue Cryopreservation

This process involves surgery, ovary removal, ovary tissue freezing, and putting ovarian tissue back into your body. This process is considered experimental and you must enter into a research study to undergo this process.

- Surgery will likely be done as a laparoscopy that uses small incisions in the abdomen to access the ovary. It is possible you may require a larger incision to remove the ovary.
- A portion of or a complete ovary will be removed on one or both sides. Removing the ovary will reduce your number of eggs you have left, and may increase your chance of infertility or early menopause in the future.
- Ovary tissue freezing involved cutting the ovary into strips that contain your eggs. These strips are then frozen and can be stored for an unlimited amount of time.
- In the future, ovarian strips will be thawed and can be replaced back into the human body for use with assisted reproductive technologies (IVF) or for natural conception. Limited information exists on the success of this process.
- Ideally, this process is reserved for women who cannot undergo egg or embryo because of cancer diagnosis, age (not having started puberty), or time.

4) Suppression of Your Ovaries during cancer treatment

This treatment involves administering a medication (Lupron or GnRH agonist) by injection every 1 to 3 months to turn off your ovaries or suppress them. Symptoms can include hot flashes, night sweats, mood changes, and vaginal dryness. The medication works by decreasing blood supply to the ovaries during your treatment to decrease the amount of chemotherapy delivered to your ovaries.

This treatment is also considered experimental and may only be beneficial for certain cancer types.

*All treatments are aimed to help preserve fertility, but unfortunately completing these treatments does not guarantee success in the future.

Fertility Options After Treatment

If you've already finished cancer treatment or you do not proceed with fertility preservation at this time, other options exist in the future. These include egg donation, gestational surrogacy, and adoption.

What Does Oocyte-Embryo Banking Entail?

Required Screening and Testing:

Preliminary screening tests are required prior to initiating an IVF cycle in order to help optimize your outcome. The tests that you may need depend on your overall general health, past health problems and any pertinent family history. The tests are intended to look for problems that could impact your chances of success with IVF treatment. Your partner will also need to have some testing done as described below. If you have had any of the tests listed below, make sure you have these records forwarded to our office. On occasion some of the tests may need to be repeated. If your medical and/or family history suggests that you may be at risk for certain inherited or autoimmune diseases, additional testing may be ordered.

Female Testing

- Ovarian Function Tests (Egg Quality)
- Hormone Testing that May Effect Oocyte (egg) Recruitment
- Radiologic Evaluation
- Infectious Disease Screening and Testing

Male (Partner) Testing

- Semen Analysis (SA)
- Blood: Infectious Disease Screening and Testing
OR
- Donor Sperm Selection**

*****If Using a Sperm Donor:***

As part of your preparation process for insemination of your oocytes (eggs) using donor sperm, you will need to select a commercial sperm bank, order your specimens and arrange for their payment and shipment to our laboratory. The UC Center For Reproductive Sciences will only accept and store semen specimens from sperm banks that have been accredited by the American Association of Tissue Banks (AATB). Such

accreditation assures us that these banks meet specific minimal standards for disease screening and semen quality.

Genetic Screening: We offer genetic screening testing and preconception testing to all patients in our practice. You may request more information regarding this now or in the future when using your gametes.

Medications: "Frequently asked Questions"

There are a number of medications that you may use during your IVF cycle. The section below lists and describes the medications that we currently use at *The Center For Reproductive Health*. From time to time new medications are introduced. We will try to keep you informed about such medications as we begin to use them in our program. If you have any questions regarding any of the medications you are using, please ask a member of our clinical staff.

Oral Contraceptives

Oral contraceptives (OCPs, birth control pills) contain both synthetic estrogen and progesterone-like compounds. OCPs are sometimes used to enhance your response to the gonadotropins and to provide us with some flexibility in scheduling and starting your IVF cycle. There are a variety of oral contraceptives on the market, many of which can be used for our purposes. If you have previously taken an oral contraceptive that you tolerated well, let us know so we can consider prescribing it for you. The length of time you will be on the OCPs may be different from other IVF patients depending upon your history and when you enter the program to start your ART cycle.

Some common side effects of the hormones in birth control pills include nausea, breast tenderness, increased appetite and weight gain, acne, increased breast size, and headaches. Though low, there are also risks associated with OCP's. These risks include stroke, deep vein thrombosis, and pulmonary emboli. If you are over 35 years of age and smoke, if you are a heavy smoker at any age or have serious heart disease you may be at increased risk for these complications. If you smoke or just recently (< 6months) discontinued, you should not take oral contraceptive pills.

Gonadotropin-Releasing hormone (GnRH) Agonist and Antagonists

GnRH agonists have been used in IVF since the 1980's to increase the number of eggs we retrieve from your ovaries and to prevent premature ovulation. GnRH antagonists have been used in IVF since late 1990's/2000. Both work to prevent premature ovulation. The agonists are typically started 7-14 days prior to starting the fertility (gonadotropin) injections, while the

antagonists typically are started after 5-8 days of being on the fertility injections. Different clinical scenarios will dictate if you are prescribed the agonist or antagonist. All patients will be on one or the other.

Lupron is a GnRH agonist that may be administered by subcutaneous injection once or twice daily. It is usually started prior to gonadotropins, and continued until you are ready for retrieval. **Risks and Side Effects of Lupron:** hot flashes, vaginal dryness, mood swings, vaginal bleeding/spotting, headaches or insomnia. All are short term and usually disappear after you start your gonadotropins. Women who use Lupron for more than 6 months may have loss of some of the density of their bones. However, you will be on Lupron less than 30 days.

Ganirelix or Cetrotide are GnRH antagonists and are also administered subcutaneously. They are used like Lupron to prevent ovulation, but are only started after gonadotropin therapy has already begun. Your individualized protocol will inform you when to start these medications. **Risks and Side Effects of Ganirelix/Cetrotide:** abdominal pain, headaches, vaginal bleeding or spotting, nausea and irritation at the injection site. All are uncommon, short term and generally disappear after you stop taking the drug.

Gonadotropins ("fertility shots") are hormones secreted by the pituitary gland and include FSH and LH. FSH is responsible for the selection and growth of developing eggs and follicles on your ovaries. LH plays an important role in the final maturation of the eggs and also causes ovulation to occur during a natural menstrual cycle.

All gonadotropins can be injected subcutaneously. Some come as a powder that must be mixed with sterile saline or water prior to their use, others come pre-mixed. Your physician will select the drug and dosages that are most appropriate for you and our clinical staff will provide you with instructions on how to use them.

- **Follistim Pen** utilizes premixed cartridges of Follicle Stimulating Hormone (FSH) and a reusable pen delivery system.
- **Gonal-F Pen** utilizes premixed cartridges of FSH and a disposable pen delivery system.
- **Bravelle (FSH)** and **Menopur (FSH + Leutinizing Hormone)** powder must be reconstituted prior to being injected with a syringe.

Adverse Reactions/Side Effects: Occasionally you may experience one or more of the following reactions to the gonadotropins you are taking:

- Local irritation at the injection site
- Dizziness, nausea, headache, mood swings, irritability, hot flashes
- Ovarian enlargement and twisting of the ovary (torsion, which is rare)

- Ovarian Hyperstimulation Syndrome (OHSS) is an excessive enlargement of the ovaries and accumulation of fluid in the abdomen. Some of the risks associated with OHSS include:
 - ✓ Deep vein thrombosis (clots)
 - ✓ Pulmonary embolism
 - ✓ Stroke

Human Chorionic Gonadotropin (hCG) is the hormone associated with pregnancy and its actions in the body are identical to LH. There are two main categories of hCG used for ART cycles, urinary and recombinant. Urinary gonadotropins, as the name implies are isolated from the urine of postmenopausal women using special processes to ensure their safety and potency. hCG medications that are urinary gonadotropins include Profasi, Pregnyl and Novarel. These medications are injected intramuscularly (IM). Recombinant hCG is a product of DNA technology and contains only pure hCG. Ovidrel is a recombinant hCG product used in some IVF cycles, but more commonly for Intrauterine Insemination (IUI) cycles. Ovidrel is a subcutaneous injection.

hCG is used in an ART cycle to mimic the normal midcycle LH surge, which is necessary to facilitate the final maturation process of the egg. The timing between your administering of hCG and the egg retrieval is carefully planned so you do not ovulate prior to us collecting your eggs at the retrieval. **Your egg retrieval is done before you ovulate your eggs.** Our clinical staff will instruct you on both the date and time you are to take your hCG.

Your treatment protocol may also include dilute or low dose hCG to add a small steady dose of LH during the growth and maturation of your follicles and eggs. Dilute hCG is administered subcutaneously using an insulin syringe and should be kept refrigerated.

Drugs Used For Oocyte Retrieval

Antibiotics are used to minimize infection from your retrieval. These include:

- Antibiotic (Z-pack, doxycycline, other) are given to patients for several reasons during an ART cycle. During micromanipulation procedures, a small hole is made in the outer covering of the egg (zona pellucida) and the antibiotics prevent bacterial contamination of the manipulated egg or embryo.

Risks and Side Effects: gastrointestinal upset, nausea, vomiting, diarrhea, phototoxicity (allergic reaction to sunlight), and allergic reaction (rash, itching, asthma). Alert our clinical staff if you have a known allergy to a specific type of antibiotic that you have been prescribed in the past so that we may avoid its usage during your IVF treatment.

Monitoring of the Cycle

The two basic methods for monitoring an ART cycle are the use of transvaginal ultrasound and measurement of hormone levels (estrogen, progesterone) in a sample of your blood.

Vaginal Ultrasounds: Ultrasound (U/S) machines use sound waves to create a visual picture of your internal anatomy. Our providers use transvaginal U/S probes to visualize both your ovaries and uterus during your ART stimulation cycle so we can assess how you are progressing and when you may be ready for your egg retrieval. The U/S probe (transducer) is gently inserted into your vagina so the ovaries and uterus can be evaluated.

Blood Tests: Estradiol is a steroid hormone that is produced by the follicles growing on your ovaries. Its main function is to mature the developing egg and stimulate the lining of your uterus to grow and thicken to make it receptive to implantation and be able to support a pregnancy.

Oocyte Retrieval

All egg retrievals are performed in our facility at in West Chester. Egg retrieval is a minor surgical procedure that is performed under deep sedation, also known as IV sedation. On the day of your egg retrieval you will come to our West Chester office and the IVF Nurses will help prepare you for your egg retrieval. We ask that you arrive at least 60 minutes prior to your scheduled procedure time so that you may change into the proper attire, complete paperwork and meet with your anesthesia provider. You will then be brought into the procedure room where you will lie on an exam table and your IV sedation will be started by an IVF Nurse.

A vaginal U/S probe along with a thin aspiration needle is then placed into your vagina and under U/S guidance the needle is inserted through the back wall of your vagina into the ovary. The physician then punctures each follicle with the needle tip and aspirates the fluid from the follicles. The fluid is collected into sterile test tubes that are passed along to the ART laboratory where the contents are screened for an egg.

The egg retrieval lasts about 20-30 minutes. You will then go to our recovery room for about 30-45 minutes and when you're completely awake and alert, you will be allowed to go home.

The egg retrieval procedure is well tolerated by the majority of patients and you should be able to go back to your usual routine the day after the retrieval. On occasion the retrieval procedure can cause mild to moderate discomfort especially in your pelvic area. While the egg retrieval is a very safe procedure, as with all surgical procedures there are possible risks including:

- 1) The attempt to recover eggs may not be successful.
- 2) Other internal organs such as the bladder, bowel or blood vessels could be injured and require further surgery (this is extremely rare).
- 3) Limited bleeding from the ovaries may occur and surgery may be required to stop the bleeding (again extremely rare).
- 4) Infections following the egg retrieval are possible, but are rare and you will be placed on an antibiotic after the egg retrieval.

In-Vitro Fertilization and Micromanipulation Insemination For Those Doing Embryo Banking

When semen has moderate or severe defects, we recommend treatment with a process of micromanipulation called **intracytoplasmic sperm injection (ICSI)** to optimize fertilization. The embryologist (egg and sperm specialist) specially prepares the sperm and a single sperm is injected into each egg. This technique greatly increases the chances that fertilization will occur. Cryopreserved eggs will need ICSI in the future for fertilization once thawed.

For Oocyte Cryopreservation

After eggs are retrieved, they are transferred to the embryology laboratory where they are kept in conditions that support their needs and growth. Eggs are placed under specialized conditions (culture media, controlled temperature, and humidity) The eggs are placed in small dishes or tubes containing "culture media," which is special fluid developed to assess if the oocytes are suitable for cryopreservation (Freezing).

Oocyte Cryopreservation Procedures

Vitrification procedure will be used to freeze your unfertilized eggs. Following vitrification, these eggs will be thawed again in the future as determined by you. Once vitrified and stored frozen, any oocytes may be kept for an unspecified period. The decision on the fate of your vitrified eggs will only be made by you.

Outcomes

There is limited data on the outcomes of using cryopreserved oocytes. Success rates be significantly lower than current estimates for women who cryopreserve oocytes after age 35, given that most published reports have described outcomes for younger women. At the time you are prepared to use your cryopreserved oocytes to help establish a pregnancy, CRH physicians will review the process and risk including ICSI, embryo transfer, outcomes data, and disposition options for excess embryos.

The long term outcome of egg freezing on embryo development is unknown. The data to date on egg freezing and subsequent pregnancies has been reassuring, and no differences have been observed between slow frozen or vitrified oocytes.

Embryo cryopreservation/banking

Freezing (or "cryopreservation") of embryos is a common procedure. As a result of multiple eggs (oocytes) being produced during ovarian stimulation, these embryos, if viable, can be frozen for future use. The pregnancy success rates for cryopreserved embryos transferred into the human uterus can vary from practice to practice. Overall pregnancy rates at the national level with frozen embryos are lower than with fresh embryos. This, at least in part, results from the routine selection of the best-looking embryos for fresh transfer, reserving the remaining ('second-best') embryos for freezing. However, there is some evidence that pregnancy rates are similar when there is no such selection as is the case with embryo banking.

Risks of embryo cryopreservation: There are several techniques for embryo cryopreservation, and research is ongoing. Traditional methods include "slow," graduated freezing in a computerized setting, and "rapid" freezing methods, called "vitrification." Current techniques deliver a high percentage of viable embryos thawed after cryopreservation, but there can be no certainty that embryos will thaw normally, nor be viable enough to divide and eventually implant in the uterus. Cryopreservation techniques could theoretically be injurious to the embryo. However, until very large numbers of children have been born following freezing and thawing of embryos, it is not possible to be certain that the rate of abnormalities is no different from the normal rate.

Pregnancy and Outcomes

Pregnancies that result from *in vitro* fertilization do not appear to be at any higher risks than any other pregnancy with the same number of fetuses. The risks of congenital abnormalities for babies born from ART compared to babies born without the use of these technologies seems to be the same, which is 2-5% of all births. Pregnancies from ART are at the same age-related risks (e.g., Down's syndrome) that occur in the general population. Data accumulated for ART pregnancies and births over the last decade (many thousands of babies) have not documented an increase incidence of fetal abnormalities or childhood anomalies compared to non-IVF babies. However, some of the technologies used in ART (e.g., micromanipulation, PGD) are relatively new and long-term data are not available. The use of ART to achieve a pregnancy does not guarantee the normalcy of any infant that may result from these procedures. Once you have a viable pregnancy you will need to continue care with your obstetrician for the remainder of your pregnancy.

Storing your Eggs or Embryos

Your eggs and/or embryos can be stored for an unlimited amount of time. If self pay, your first year of storage is included in the cost of your fertility preservation package. In using insurance, insurance will not pay for you storage costs, so this payment for 1 year of storage will be due at time start of your cycle. After 1 year you have the option to continue to store at the UC Center for Reproductive Health for an annual fee (please see pricing information) or you can choose to send them to long-term storage. To avoid a charge for annual storage you will need to contact our office prior to 1 year time point from your initial freezing of eggs or embryos. Long-term storage costs are reduced at Cryopoint (please see included consent form and contact information) for cancer patients. You will be responsible for all charges for shipping and storage at the long-term facility.



Ovarian Tissue
(OncoFertility)

Dear Client Depositor,

ReproTech, Ltd. (RTL) is pleased to have been selected by the Oncofertility Consortium as the facility to assume the storage responsibilities of your cryopreserved ovarian tissue. ReproTech, Ltd. is proud to be licensed by the New York State Department of Health, the State of California Department of Health Services and accredited by the American Association of Tissue Banks. Our staff will provide you with the highest level of experience and professionalism to service your needs.

Our annual storage fee is \$275 and the transfer fee to ship a tank from your clinic to ReproTech is \$215. (You also have the option of paying annually, quarterly, or at our multi-year rates.) If you apply for ReproTech's financial assistance program (Verna's Purse) and are approved, the annual fee will be reduced to \$75, and the transfer fee will be reduced to \$95. The fee for the first storage period and the transfer fee must be prepaid before the tank is shipped to your clinic.

Once we receive this paperwork from you or your clinic, we can arrange a transfer.

- A. **Client Depositor Registration;**
This form gives us information about you, the Client Depositor. Please provide a credit card for the storage and transfer fees. Regardless of the method chosen, this form needs a signature on the bottom, indicating that you accept and understand our billing policy.
- B. **Oocyte/Ovarian Tissue Cryostorage Agreement;**
Please read this agreement carefully. Sign this form in the presence of a witness. Upon witnessing your signature, the witness will need to sign the form as well.
- C. **Specimen Transfer To RTL And Medical Data Release Authorization;**
This form must be signed by you, the Client Depositor, in the presence of a witness. The witness must also sign the form. This form allows us to get your serology results from your IVF clinic. We will have your IVF clinic complete the bottom portion of this form at the time of the transfer. If you wish to purchase insurance for the shipment, please read enclosed Specimen Shipping Insurance form and check the appropriate box on the form.
- D. **Addendum To Oocyte Cryostorage Agreement;**
Please read this agreement carefully. You must sign this form in the presence of a witness. This form is required in the event that a reactive test result is on file, or no serology results are available at the time of transfer to RTL.
- E. **HIV-1/2 (AIDS) Testing;**
Prior to transfer, RTL requires evidence of your serology for Anti-HIV-1/2(AIDS). These testing results can be provided by your clinic or other testing facility.

In compliance with AATB Standards and RTL policies, the following tests must be completed and the results forwarded to RTL prior to release of your ovarian tissue for your use in the future: Anti-HIV-1/2, HBsAg, and HCV.

Please call RTL at 888-489-8944 if you have any questions or visit our website at www.reprotech.com. We will notify you via mail once a transfer has occurred and your ovarian tissue is in storage at ReproTech, Ltd.

Sincerely,
Ben Hackner

The Cryostorage & Compliance Experts

NV 888.831.2765 • MN 888.489.8944 • FL 888.953.9669 • TX 888.350.3247



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Fertility Preservation Discounted Case Rate OncoFertility

The Global Cash Discount Package has been created to provide you an affordable, inclusive fee for In-Vitro Fertilization. The discount is based on upfront payment due before calendar dates are given. If payment is not received in full, your cycle will be delayed.

Professional Services for Oocytes Only	\$5500.00
Professional Services for Oocytes and Embryos	\$7500.00

Professional / Laboratory Services Included

Cycle Monitoring:

Office Visits, Ultrasounds, Telephone Visits, Cycle, Reviews/Management, IVF Cycle Education

Blood Work for Cycle:

Venipuncture, E2 (estradiol), P4 (progesterone), HCG (Pre-cycle Pregnancy Test)

IVF Retrieval for Oocytes:

Anesthesia, Retrieval, IVF Lab Services (Identification of Oocyte's, Culture, and Prep to freeze), All Surgical Supplies, Recovery, Oocyte Cryopreservation, One year of Free Storage

IVF Retrieval for Oocytes and Embryos:

Anesthesia, Retrieval, Embryology Lab Service: Identification and Insemination, Culture Oocytes and Embryo' and Sperm Prep if necessary. All Surgical Supplies, Recovery, Oocyte/Embryo Cryopreservation, and One year of Free Storage

**Cost Excluded from Cycle:

Medications are not included in the cost of the IVF cycle.

FDA labs and screening are available at request for a separate fee of \$300.

The Physicians at the Center for Reproductive Health are committed to the necessary care for a successful cycle. In the event the patient's cycle is canceled by the attending physician due to poor response or hyper response, and to maintain the health of the patient, the patient will be responsible to pay a fee for service case rate for monitoring visits.

Services provided prior to payment of any infertility cycle, will be the responsibility of the patient in the event the patient decides not to move forward with the planned infertility cycle.