University of Iowa Hospitals & Clinics

Center for Advanced Reproductive Care

Fertility Preservation

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INTRODUCTION

The aim of this booklet is to provide you with an overview of fertility preservation, with an emphasis on those services available here at UIHC. If you think you may be interested in any of these services and would like more information, please schedule an appointment with us in our IVF clinic (319-356-8483) so that we can provide you with more one-on-one counseling specific to your needs. We may then recommend an appointment in either our IVF or Reproductive Endocrinology clinics.

Fertility preservation services available at the UIHC Center for Advanced Reproductive Care include:

- Comprehensive fertility evaluation of the individual or couple
- In vitro fertilization with embryo cryopreservation
- Preimplantation genetic diagnosis
- Anonymous and known oocyte donation
- Anonymous and known embryo donation
- Anonymous and known sperm donation
- Assisted fertilization via ICSI
- Sperm retrieval
- Sperm cryopreservation
- Counseling services

Patients who might consider fertility preservation options include:

- Cancer patients
- Women with benign ovarian disease or endometriosis requiring extensive surgery
- Women with BRCA I and II mutations
- Autoimmune disease patients
  (such as lupus nephritis, acute glomerulonephritis, behcet's syndrome)
- Patients with hematologic diseases
  (ie Sickle Cell disease)
- Women at increased risk for premature ovarian failure
  (Fragile X premutation carriers, family history of early menopause)

UNDERSTANDING FERTILITY PRESERVATION

It is important for you to be aware of what impact your diagnosis and treatment will have on your reproductive health before beginning treatment, and what options are available to you to preserve your fertility. The following information can be used as a guide to initiate a meaningful discussion with your physician. Much of this information refers to the diagnosis of cancer, but it can also be applied to the conditions on the previous page which may involve the same treatment.

What impact will my diagnosis and treatment have on my fertility?
Cancer itself usually does not affect fertility in women. It is the treatment of cancer, which can be the same treatment used for some benign conditions, which affects fertility. One of the most important factors in determining the impact of your diagnosis and treatment on your fertility is your fertility status prior to treatment. Most of the time, patients are unaware of their fertility status prior to treatment. Regular menstrual cycles or a prior pregnancy does not always indicate fertility. A Reproductive Endocrinologist can help you determine your current fertility status. Age is an important factor in predicting fertility, with a significant decline in women around the age of 37 or 38. Ovarian reserve is also a useful indictor, which is often estimated by looking at the ovaries using transvaginal ultrasound images. The size of the ovaries and the number of follicles present (egg-containing cysts) indicate the number of eggs remaining in the ovaries (ovarian reserve). An FSH level on the third day of your menstrual cycle is also commonly used to measure ovarian reserve. AMH (anti-mullerian hormone) may be a useful marker in the future, but currently more research is needed. We would strongly encourage you to have an evaluation of your ovarian reserve prior to starting any cancer treatment so that you can be more accurately counseled on the impact of your cancer treatment on your fertility and the success of various fertility preservation options.

The specifics of your treatment (ie chemotherapy, radiation, surgery) will also determine your risk for infertility. Chemotherapy and radiation can damage the cells that produce eggs and sperm, but the extent to which this occurs depends on several factors. With regard to **chemotherapy**, the most important issues will be the type of chemotherapy agent and the cumulative dose. Certain chemotherapy agents are more damaging than others. Alkylating agents, like cyclophosphamide and procarbazine, tend to have a much greater effect on ovaries than other agents like methotrexate, vincristine, and bleomycin which have little effect. **Radiation** can be particularly toxic to ovaries if it is directed toward your pelvic area. In general, a single high dose is worse than several smaller fractionated doses. Shielding the ovaries may help minimize the effects. Radiation can also damage the uterus and increase the risk of miscarriage and low birth-weight. Radiation to the pituitary gland or hormone-producing areas of your brain can also cause infertility by interfering with your normal hormone production. **Surgery** to remove reproductive organs such as the ovaries, fallopian tubes, uterus, and/or cervix will impair the ability to become pregnant and/or carry a baby. **Bone marrow and stem cell transplants** generally involve high doses of chemotherapy, sometimes combined with full body radiation.
Table 1 is a compilation of both clinical experience and published research on the impact of common cancer treatments on menstruation. There are a lot of abbreviations in this table which may not be clear. It may be helpful to review this table with your oncologist so they can show you what treatment protocol they are recommending for you. Keep

in mind that this table, along with much of the published research in this area, defines infertility as amenorrhea, which means loss of menstruation. This may underestimate the risk of infertility. Many women who return to menstruation after the completion of treatment mistakenly believe their reproductive capacity has not been affected. This is a common misconception. You should be aware that women with regular menstrual cycles may still be infertile and may also be at risk for going through menopause much earlier.

For men, exposure to **chemotherapy** and/or **radiation** compromises sperm production, quality, motility and DNA damage. As with women, factors determining the likelihood of reproductive damage for men include: drug type and dosage; radiation location and dosage; patient's pubertal status at time of treatment; and patient's pre-treatment fertility (which is often unknown). **Table 2** is a compilation of clinical experience and current research on common cancer treatments on the risk of azoospermia, which means that no sperm are found in the ejaculate. **Surgery** on the testes or in the pelvis can also affect sperm production or can damage the nerves that cause ejaculation.

What is the safety of pregnancy for me?

You should be aware of any increased risks you might have in the future with pregnancy due to your diagnosis and treatment. For example, it appears that radiation (but not chemotherapy) puts patients at increased risk for miscarriage, preterm labor, preterm delivery, low birth weight, and placenta accreta (abnormal implantation of the placenta). Many types of chemotherapy, such as doxorubicin, are associated with long-term cardiovascular complications which may put you at significantly increased risk during pregnancy. If you have been exposed to such agents, you should have a cardiac evaluation prior to pregnancy.

Cancer recurrence. With the possible exception of gestational trophoblastic disease, pregnancy does not appear to affect the risk of recurrence of any type of cancer, with melanoma and breast cancer being the best studied cancers. To date the effect of subsequent pregnancy after breast cancer on prognosis and survival is reassuring. In fact, several studies have shown a favorable effect, consistent with a possible protective effect of the pregnancy. While these studies are reassuring, the issue still remains controversial, as many of these studies are limited by small size and confounding factors. Breast cancer patients should wait at least two years before pregnancy, primarily because this is when most recurrences will occur. However, should you get pregnant prior to then, there is no evidence to suggest that you should terminate the pregnancy.

Cancer treatments. Some cancer treatments, such as methotrexate, have a long half life and can be retained for several months in the liver. Pregnancy should therefore be avoided for 3 months after stopping MTX.

Breast feeding. Most women who have undergone irradiation for breast cancer are able to produce small amounts of milk on the affected side, but the amount of milk produced may be less and mastitis would be difficult to treat if it occurs. However, milk production from the contralateral breast is not affected by previous or concurrent irradiation and is safe.

TABLE 1. Risk of Amenorrhea (loss of menses)
From chemotherapy and radiation treatments for cancer

Degree of Risk	Treatment Protocol	Common Usage
High Risk >80% of women develop amenorrhea post-treatment	Whole abdominal or pelvic radiation doses ≥6 Gy in adult women	Multiple cancers
	Whole abdominal or pelvic radiation doses ≥15 Gy in pre-pubertal girls ≥10 Gy in post-pubertal girls	Wilm's tumor, neuroblastoma, sarcoma, Hodgkin lymphoma
	TBI radiation doses	Bone marrow transplant/stem cell transplant
	CMF, CEF, CAF X 6 cycles in women 40+	Breast cancer
	Cyclophosphamide 5 g/m² in women 40+	Multiple cancers
	Cyclophosphamide 7.5 5 g/m² in girls <20	Non-hodgkin lymphoma (NHL), neuroblastoma, ALL, sarcoma
	Alkylating chemotherapy (e.g., cyclophosphamide, busulfan, melaphan) conditioning for transplant	BMT/SCT
	Any alkylating agent (e.g., cyclophosphamide, ifosfamide, busulfan, BCNU, CCNU) + TBI or pelvic radiation	BMT/SCT, ovarian cancer, sarcoma, neuroblastoma, Hodgkin lymphoma
	Protocols containing procarbazine: MOPP, MVPP, COPP, ChlVPP, ChlVPP/EVA, BEACOPP, MOPP/ABVD, COPP/ABVD	Hodgkin lymphoma
	Cranial/brain radiation ≥40 Gy	Brain tumor
Intermediate Risk ~30-70% of women develop amenorrhea	CMG or CEF or CAF X 6 cycles in women 30-39	Breast cancer
	AC in women 40+	Breast cancer
	Whole abdominal or pelvic radiation 10-15 Gy in prepubertal girls	Wilms' tumor
	Whole abdominal or pelvic radiation 5-10 Gy in postpubertal girls	Wilm's tumor, neuroblastoma
	Spinal radiation ≥ 25 Gy	Spinal tumor, brain tumor, neuroblastoma, relapsed ALL or NHL
Low Risk <20% of women develop amenorrhea	AC in women 30-39	Breast cancer
	CMF, CEF, or CAF X 6 cycles in women under 30	Breast cancer
	Non-alkylating chemo: ABVD, CHOP, COP	Hodgkin lymphoma, NHL
	AC (anthracycline, cytarabine)	Acute myeloid leukemia (AML)
	Multi-agent therapies	ALL
Very Low Risk Negligible effect on menses	MF (methotrexate, 5-FU)	Breast cancer
	Vincristine (used in multi-agent therapies)	Leukemia, Hodgkin lymphoma, NHL, neuroblastoma, rhabdomyosarcoma, Wilms' tumor, Kaposi's sarcoma
	Radioactive Iodine	Thyroid cancer
Unknown Risk	Paclitaxel, docetaxel (taxanes used in AC protocols)	Breast cancer
	Oxaliplatin	Ovarian cancer
	Irinotecan	Colon cancer
	Bevacizumab (Avastin)	Colon, non-small cell lung
	Cetuximab (Erbitux)	Colon, head & neck
	Trastuzamab (Herceptin)	Breast cancer
	Erlotinib (Tarceva)	Non-small cell lung, pancreatic
	Imatinib (Gleevec)	Chronic myeloid leukemia (CML), gastrointestinal stromal tumor (GIST)

TABLE 2. Risk of Azoospermia (no sperm in ejaculate)
From chemotherapy and radiation treatments for cancer

Degree of	Treatment Protocol	Common Usage

Risk		
High Risk Prolonged azoospermia	Total body irradiation (TBI) Testicular radiation dose >2.5 Gy in men Testicular radiation dose ≥ 6 Gy in bosy Protocols containing procarbazine: COPP, MOPP, MVPP, ChlVPP, ChlVPP/EVA, MOPP/ABVD, COPP/ABVD Alkylating chemo for transplant conditioning (cyclophosphamide, busulfan, melphalan) Any alkylating agent (e.g. procarbazine, nitrogen mustard, cyclosphosphamide) + TBI, pelvic radiation, or testicular radiation Cyclophosphamide >7.5 g/m^2 Cranial/brain radiation ≥ 40 Gy	Bone marrow transplant/stem cell transplant (BMT/SCT) Testicular cancer, ALL, non-Hodgkin lymphoma ALL, NGL, sarcoma, germ cell tumors Hodgkin lymphoma BMT/SCT Testicular cancer, BMT/SCT, ALL< NHL, sarcoma, neuroblastoma, Hodgkin lymphoma Sarcoma, NHL, neuroblastoma, ALL Brain tumor
Intermediate Risk Prolonged azoospermia not common at standard dose	BEP x 2-4 cycles (bleomycin, etoposide, cisplatin) Cumulative cisplatin dose <400 mg/m^2 Cumulative carboplatin dose ≤ 2 g/m^2 Testicular radiation dose 1-6 Gy (due to scatter from abdominal/pelvic radiation)	Testicular cancer Testicular cancer Testicular cancer Wilms' tumor, neuroblastoma
Low Risk Temporary azoospermia	Non-alkylating chemotherapy: ABVD, OEPA, NOVP, CHOP, COP Testicular radiation dose 0.2 -0.7 Gy	Hodgkin lymphoma, NGL Testicular cancer
Very Low Risk No effects on sperm production	Testicular radiation dose < 0.2 Gy Interferon-alpha Radioactive iodine	Multiple cancers Multiple cancers Thyroid
Unknown Risk	Irinotecan Bevacizumab (Avastin) Cetuximab (Erbitux) Erlotinib (Tarceva) Imatinib (Gleevec)	Colon Colon, non-small cell lung Colon, head & neck Non-small cell lung, pancreatic Chronic myeloid leukemia (CML), gastrointestinal stromal tumor (GIST)

What fertility preservation options are available to me?

Fertility preservation is a very new and emerging field, so many of the options currently available are still considered experimental. Nevertheless, you should make yourself aware of all of these options so that you can make an informed decision. Here we will review each one, explain the process, describe who may or may not be a good candidate, and review the success, cost, risk, and availability.

- **Embryo cryopreservation (freezing)** *
- **Preimplantation genetic diagnosis** *
- **Oocyte cryopreservation (freezing eggs)** **
- **Ovarian tissue cryopreservation**
- **Ovarian suppression** *
- **Sperm cryopreservation** *
- **Sperm retrieval** *
- **Radiation shielding of gonads** *
- **Ovarian transposition** *
- **Donor embryos and oocytes, and sperm** *
- **Gestational surrogacy** **
- **Adoption**

* Currently available here at UIHC
** may be available soon at UIHC

Embryo Cryopreservation (Embryo freezing)

Embryo freezing prior to cancer treatment currently offers patients who require fertility preservation the highest likelihood of a future pregnancy.

The Process

In general, embryo cryopreservation involves fertilizing eggs with sperm in a lab through in-vitro fertilization (IVF) and then freezing the embryos that are created. The process begins with "Ovarian Hyperstimulation", whereby women are given medication to stimulate the production of eggs by their ovaries. Typically, daily self-administered injections of hormones are given for approximately 8-12 days, while response to the medication is monitored with frequent blood work and ultrasounds. The process sometimes takes up to 5 weeks, depending on the use of medication prior to the stimulation and the onset of your period. Side effects may include bloating, discomfort, and mood changes. When your ovaries are ready, you will undergo a procedure called "Oocyte Retrieval". This is an outpatient procedure done under IV sedation where eggs are retrieved from you ovaries with a needle that is directed through your vagina over an ultrasound probe. The procedure usually takes about 20 minutes, and complications are rare. Once removed, the eggs are fertilized in the lab with sperm to create embryos. The embryos that develop successfully are then frozen for future use. When you are ready to conceive, the embryos are thawed and placed back into your uterus in a procedure called "Embryo Transfer". You will likely have to take medications for several weeks to build the lining of your uterus so that the embryos will implant. Following the transfer, you would continue to take hormone support in the form of progesterone injections for 12 weeks, if you are pregnant. Even if you are infertile or in menopause, you can carry a baby using your frozen embryos as the uterine lining can usually be prepared with medication. If your uterus has been removed or damaged from treatment, the embryos may be transferred into a gestational carrier. Frozen embryos are usually stored as small groups in separate vials, so that you do not have to thaw and use them all at the same time. For example, if you have ten embryos frozen, you may decide to thaw three the first time that you try. Not all of the embryos that are thawed will survive. Generally between one and six are thawed and between one and four are transferred. The number of embryos that we transfer into your uterus at one time will depend on your age (at the time of retrieval) and the quality of the embryos.

The Patient

Embryo freezing requires both eggs and sperm, so this option is predominantly suitable for patients with a partner. However, if you are a single woman, the use of donor sperm is an option. We do not consider donor sperm an appropriate option for very young women or teenagers.

Success

The success of IVF depends on multiple factors, the most important being maternal age at the time of oocyte retrieval, and egg quality and quantity. Generally women under age 35 have good quality eggs. Here at UIHC, our success rates for frozen IVF cycles on infertile couples (without cancer) from 2005-2007 are the following:

Age (at time of egg retrieval)	Ongoing pregnancy rate per transfer
<35	51%
35-37	32%
38-40	46 %
41-42	10 %

For comparison purposes, the success rate of natural conception between a fertile man and women is 20-25% per cycle. We can give you a better idea of your chance of success after a thorough evaluation. We often have to use different types of stimulation protocols in cancer patients, which can decrease the response. The chance of pregnancy will also depend heavily on the number of embryos you have to freeze, as that will determine how many transfers, or attempts, you would have in the future. Generally, ~ ¾ of embryos will survive the freezing and thawing process, so realistically you may only freeze enough embryos for one transfer. Ideally, a patient would undergo more than one "fresh" cycle in order to store more embryos in case one cycle is not successful. The downside of this is that it would further delay the initiation of your cancer treatment. Excess frozen embryos that you do not use can be discarded, donated to another couple, or donated to research. All cryopreserved embryo transfers must be completed by your 50TH birthday.

Risks

The main risk to cancer patients of this option is the delay in cancer treatment. In women with hormone-sensitive tumors such as breast and endometrial cancer, there is the additional concern regarding the safety of ovarian stimulation, as high levels of estradiol are sometimes reached. Women with breast cancer have a unique situation since there is typically six weeks from surgery to chemotherapy which is adequate to complete an IVF cycle. However, many breast tumors contain estrogen receptor positive cells, which might be adversely affected by high estradiol levels. Alternative stimulation protocols can be used in these situations, which may include tamoxifen, a medication commonly used to treat breast cancer. Another risk associated with the stimulation includes the development of ovarian hyperstimulation syndrome, which can cause abdominal pain and distention, enlarged ovaries, fluid retention, and shortness of breath. This can be life threatening, but here at UIHC <1% of patients require hospitalization for this. The possible link of ovarian cancer resulting from ovarian stimulation for IVF is unclear. The small increased risk shown in some studies may be attributed to infertility and nulliparity (no children), which are known risk factors for ovarian cancer. Risk of complications from the egg retrieval here at UIHC is <0.5%, and include bleeding, infection, and damage to other pelvic structures. Risks associated with the transfer would include multiple gestation (twins, triplets, and higher), miscarriage (10-30% of pregnancies), and ectopic pregnancy (a pregnancy outside of the uterus, 1-3% of pregnancies). Some studies have shown that birth defects are higher following IVF. The largest American study on birth defects with IVF was done here at UIHC. We found a birth defect rate of 6% in children conceived by IVF, versus 4% in naturally conceived children. Births from frozen embryos do not appear to have a higher rate of birth defects than fresh IVF cycles. However, fresh and frozen embryos can contain defects which are not apparent even after microscopic examination. Finally, an important risk to consider is the emotional one, if pregnancy does not occur.

Costs

IVF costs ~ $ 10,000 per cycle here at UIHC, with $2,000 – 5,000 more in medications. The IVF lab here will store frozen embryos for two years, free of charge. Storing embryos beyond that costs ~ $ 240 / year.

Availability

IVF with cryopreservation of embryos is no longer considered experimental and is readily available here at UIHC. (Typically IVF is scheduled during one of our 6 week long "up times" through the year.) If you think you may be interested in IVF, please contact us as soon as possible so that we can (facilitate getting you in to the next uptime and) minimize delay of your cancer treatment.

Preimplantation genetic diagnosis (PGD)

If your tumor is part of an inherited syndrome or predisposition, your offspring may be at increased risk for cancer. Preimplantation genetic diagnosis is available for many of these mutations, which would allow you to undergo IVF and only have embryos transferred which did not carry that mutation. This process involves biopsying the embryos and then testing those cells for certain genetic defects. There are several risks associated with this process, including damage to the embryo and errors in the testing (false positives as well as false negatives). We recommend strong consideration be given to amniocentesis or other prenatal testing if a pregnancy occurs following PGD, to confirm the child is not affected by the disease. Some cancer mutations for which this technology is currently available include:

- BRCA1
- BRCA2
- Familial adenomatous polyposis
- Gorlin syndrome
- Lynch/hereditary non-polyposis colon cancer
- Li-Fraumeni syndrome
- Neurofibromatosis
- Retinoblastoma
- Tuberous sclerosis
- Von Hippel-Lindau disease
- Multiple endocrine neoplasia (MEN)

Oocyte Cryopreservation (Egg Freezing)

Oocyte cryopreservation is an experimental fertility preservation option whereby eggs are removed from your body and frozen (unfertilized) for later use.

Process

Oocyte cryopreservation would begin with ovarian hyperstimulation and oocyte retrieval, as described above for embryo freezing, and would require 2-5 weeks. However, the eggs are not fertilized with sperm, but are immediately frozen. When you are ready to use the eggs, they are thawed and then fertilized with your partner's sperm or donor sperm to using intracytoplasmic sperm injection (ICSI) to create embryos. Finally, the resulting embryos are transferred into your uterus as described above.

Patient

Oocyte cryopreservation is for women who either do not have a partner, do not want to use donor sperm, or have ethical or religious objections to embryo freezing.

Success

In contrast to freezing embryos, freezing eggs has proven to be quite difficult. This is mostly because eggs contain a lot of water, which forms ice crystals during the freezing process, damaging the egg and its chromosomes (genetic material). While it is difficult to compare them side by side, pregnancy rates remain less than those with IVF and embryo freezing. However, the technology is improving rapidly. One recent study compiling the results of all egg freezing data showed that the live birth rate per embryo transfer using frozen eggs is 21.6% (compared to the average live birth rate with fresh eggs at 43.3%) for

women under the age of 35 in 2005 in the United States. However, the live-birth rate per oocyte thawed is likely to be between 2 and 4%. Success rates may be significantly lower than current overall estimates for women who cryopreserve oocytes after age 35, given that most published reports have described outcomes for younger women. Other factors that will predict success include number of eggs retrieved and quantity and quality of embryos created.

Risks

Risks are the same as those associated with embryo freezing, and include delay of cancer treatment, risk of stimulating hormone sensitive tumors, ovarian hyperstimulation syndrome, and multiple gestations. There may be unique risks related to the cryopreservation and thawing of oocytes, but this is unclear at this time.

Costs

The average cost of egg freezing is $8,000 per cycle. Medications are additional and can range from $2,000 to $5,000. Oocytes are stored free of charge for two years. Beyond that, storage would cost ~$240 / year. Fertilization with ICSI and transfer of the embryos will cost an additional $3,000.

Availability

Currently oocyte cryopreservation is not available here at UIHC. However, this is a rapidly evolving area and is something we hope to have available for our patients in the near future.

Ovarian tissue cryopreservation

Process

Ovarian tissue freezing is an experimental procedure in which doctors remove part or all of an ovary and freeze it for later use. This removal is often done laparoscopically in an outpatient surgical procedure. The tissue that is removed contains hormone-producing cells and immature eggs. When the tissue is later thawed, it can be retransplanted in one of two ways. In an "orthotopic" transplant, the tissue is put back close to where it was removed from the pelvis. Conception can then be accomplished with IVF or naturally.

Patient

Ovarian tissue freezing is an appealing option as it requires a minimum amount of time (one day for surgery). This may be suitable for women who do not have time to do embryo or egg freezing or cannot use fertility medications. It is also the only option available for prepubescent girls. Women whose cancer has spread to the ovaries may not be candidates for this option, as retranplanting the tissue would put them at risk for cancer recurrence.

Success

This is very new technology, and therefore it is difficult to estimate your chance of success. Only 4 births world-widehave been reported to date using this technology.

Risks

One limitation of this technique is that the ovarian tissue is often unable to develop a blood supply after it is transplanted. There is also concern that stored ovarian tissue could contain cancer cells which could potentially lead to a recurrence of you tumor if transplanted back.

Costs
Generally this technique costs ~$12,000 for the initial surgery to remove the ovarian tissue, $10,000 to $15,000 to transplant it back, and then possibly IVF at $10,000.

Availability
This technology is not currently available here at UIHC.

Ovarian suppression

Process
This method involves use of a medication, typically GnRHa (Gonadotropin Releasing Hormone Agonist), to suppress the ovaries while undergoing chemotherapy. The theory is that by shutting down the ovaries during chemotherapy, the damage to the follicles may be minimized. The medication is usually given as an intramuscular injection at least a week before cancer treatment begins so that it can take effect before chemotherapy starts. Since it is shutting down your ovaries, it can cause side effects common in menopause such as hot flashes and vaginal dryness. These symptoms are temporary, as GnRHa does not cause permanent menopause.

Patient
This is an option for post-pubertal women undergoing chemotherapy. Research clearly shows that GnRHa does not provide protection when very high doses of cancer drugs or radiation therapy are used. They also do not protect the ovaries from radiation.

Success
Studies looking at the success of this option have all been very small and the results have varied significantly. Some show a benefit, others do not. Properly designed studies (large randomized controlled trials) to answer this question are currently underway.

Risks
There is concern that these mediations can alter the response to chemotherapy for hormonally-sensitive cancers, like breast cancer.

Costs
The cost of this medication is approximately $500 per injection and it is usually given monthly.

Availability
This medication can be ordered by your oncologist or ob/gyn or by a fertility specialist.

Sperm cryopreservation
For men, the most proven and successful method of fertility preservation is sperm cryopreservation (freezing).

Process
Typically this involves collection of semen by masturbation in our Reproductive Testing Lab. To maximize the number and quality of sperm, we would recommend that you abstain from sexual activity for 2-7 days prior to semen collection. The semen sample must be collected into a special sterile container provided by the Reproductive Testing Laboratory. Masturbation is the preferred collection method. We have a private room set aside in the lab for collection. A semen analysis is completed approximately 45 minutes after the specimen arrives at the laboratory. We evaluate the ejaculate volume, seminal fluid consistency, sperm count, and sperm motility. Following the analysis, the semen is diluted with a cryoprotectant to protect the sperm during cryopreservation and the specimen is transferred to

cryovials. The sperm are then frozen in a controlled rate freezer and stored in a liquid nitrogen tank at -196 C. Sperm may be stored at this temperature indefinitely. When the sperm is later thawed, it can be used for intrauterine insemination (IUI) or for IVF.

Patient
Post-pubertal male patients requiring fertility preservation.

Success
The success of sperm cryopreservation depends on the quality of the specimen that is frozen. We can give you a better idea of this once we have reviewed your semen analysis.

Risks
There is little to no risk associated with sperm cryopreservation.

Costs
Semen analysis and cryopreservation cost $240. Storage of frozen sperm is approximately $150 per year.

Availability
Please contact the UIHC Reproductive Testing Lab to schedule an appointment for sperm semen analysis and sperm cryopreservation, at (319) 384-8354.
Cryogenic Laboratories, Inc., also offers a convenient "Priority Male" service, which allows men to collect at home and overnight ship the specimen to their cryobank for storage. (see Resources)

Ovarian transposition

Process
Ovarian transposition is an outpatient surgical procedure where your ovaries are surgically moved higher up into your abdomen away from the radiation field to minimize exposure and damage. It can be done in both pre- or post- pubertal patients. If you are also receiving chemotherapy, this may not be of as much benefit. The ovaries can be removed from the radiation field laparoscopically, but this should be done close to the time of radiation treatment, so that the ovaries do not have time to move back into the radiation field. So even if you have a staging laparotomy, if you are not going to have radiation for several months, it may be worthwhile to come back for laparoscopic transposition immediately before treatment.

Patient
Pre- or post-pubertal patients planning to receive pelvic radiation.

Success
Success rates of this technique have been inconsistent, varying between 16 and 90%, depending on the amount of radiation that has scattered, the radiation dose, the age of the patient, and whether the ovaries are also shielded. Because the ovaries can remigrate, spontaneous pregnancies have occurred without repositioning the ovaries, so typically they are repositioned only if difficulty conceiving occurs.

Risks
When the ovaries are moved, their blood supply may be compromised, and this could lead to decreased function or chronic pain. If the ovaries migrate back into the field, they may still receive some radiation. There may also be a risk of having difficulty diagnosing ovarian cancer if the ovaries are no longer palpable on pelvic exam.

Costs

Often ovarian transposition can be done in conjunction with other surgical procedures and therefore may be covered by insurance.

Availability
This option is currently available here at UIHC.

Donor oocytes and embryos

If you are infertile or in menopause after cancer treatments, but would like to carry a pregnancy, the use of donor oocytes or donor embryos might be good options to consider. Egg and embryo donation would allow you to still experience pregnancy and childbirth, though you would not have any genetic relationship to the child.

Process
Most often, donated embryos come from another couple who have undergone IVF. Excess embryos are frequently frozen during IVF, and if the couple chooses not to use their excess embryos, they may decide to donate them to another couple. Donor eggs can be donated to you from a known donor, for example a friend or relative, or an anonymous donor. Egg donors can be found through our IVF clinic here at UIHC. We can assist you in finding a donor based on physical characteristics, ethnic background, educational background, or other criteria that you may value. Most egg donors are between 21 and 34 years old and have undergone basic psychological, medical, and genetic screening. The eggs are retrieved from the donor and fertilized with sperm from your partner. Then the embryos are transferred into your uterus. We currently do not offer the creation of embryos from both donor eggs and donor sperm. With either embryo or egg donation, you would take medications to build the lining of your uterus so that the embryos will implant and grow. Following the transfer, you would continue to take hormone support in the form of progesterone injections until 12 weeks, if you are pregnant. We do require patients to meet with our health psychologist prior to using donor eggs or embryos.

Patient
Any women with a viable uterus who can sustain a pregnancy can try IVF with donor embryos or eggs. We do have some age limits here at UIHC, which include:
Age limits for donor embryo recipients:
- Frozen cycles: <50

Age limits for donor egg recipients are:
- Fresh cycles: <48 for anonymous donor eggs
  <50 for known donor eggs
- Frozen cycles: <50 for anonymous or known donor eggs

Success
The success of IVF using donor embryos will depend on the quality and quantity of the embryos chosen. Use of egg donation to achieve pregnancy has the highest success rates of any assisted reproductive technology, and at UIHC the pregnancy rate is about 65%.

Risks
The main risk associated with this technology is multiple pregnancies, such as twins, triplets, or higher. We will try to minimize that risk to you by limiting the number of embryos we transfer. There is also a risk of miscarriage and ectopic pregnancy.

Costs
The price of a donor egg cycle averages $21,000 for known donors, and $19,000 for anonymous donors. This includes the donated eggs, costs of fertility treatments, and medications. The cost of a donor embryo cycle is $5,800.

Availability
Embryo and egg donation is available here at UIHC.

Donor Sperm

Process
Donor sperm can be used for in-vitro fertilization or intrauterine insemination. Major sperm banks in the United States collect sperm from young men who go through a detailed screening of their physical health, educational and emotional history, family health history, and even some genetic testing. Donor sperm samples are frozen and sperm donors are retested after six months, before the donor sperm is released, to prevent disease transmission. Couples can choose a donor who matches their physical traits, educational record or talents. Couples can choose a donor who will remain anonymous or who is willing to have contact with a child later in life. You will select a donor, pay for the sperm, and then have the sperm transported to our facility. For the woman in the couple, it usually involves intrauterine (or artificial) insemination, usually without any hormone treatments. However, occasionally the woman will also need to be treated with medication or IVF. As with donor eggs or embryos, we would require that you meet with our health psychologist prior to using donated sperm for family building.

Patient
Donor sperm is the most simple and inexpensive way to become a parent for men who are infertile after cancer.

Success
Success rates range from 50-80% and are highest in women with no infertility problems. Most women become pregnant within 3 to 6 attempts.

Risks
There is a less than 1% risk of developing an infection in the uterus and/or fallopian tubes with any IUI procedure (this is unrelated to screening for the various infections discussed above).

Costs
The cost of donor sperm varies among sperm banks and depends on what combination of products and services you want, but generally ranges between $200 and $500 per vial. The Reproductive Testing Laboratory at UIHC charges a fee for storing specimens over 6 months which is currently $150 per year and is pro-rated during the first year. Intrauterine (or artificial) insemination costs ~$180-260. Additional fees would apply for any medications or procedures necessary for the female partner to conceive.

Availability
IVF or IUI with donor sperm is a service available here at UIHC. We are willing to work with any sperm bank that complies with FDA regulations governing reproductive tissue banks (21 CFR Part 1271), but we can provide you with names and contact information for sperm banks that we recommend.

Surrogacy / Gestational carriers

Process

Traditional surrogacy is when a fertile surrogate mother is artificially inseminated with the male partner's sperm. The child will have the genes of the male and the surrogate female. The female partner then usually has to adopt the baby after birth. Gestational carrier is when a woman carries a pregnancy for you, but has no genetic relation to the child. The child is the genetic offspring of the couple, not the surrogate.

Patient

Surrogacy is an option for women who are not able to carry a pregnancy (usually due to problems with their uterus or general health).

Success

Success rates are about the same as standard IVF.

Risks

Risks to you would include those associated with ovarian hyperstimulation, if you are the source of the oocytes.

Costs

The costs of surrogacy can vary greatly, ranging from $10,000 to $100,000.

Availability

Currently, surrogacy and gestational carrier are not available options here at UIHC, due to the status of the Iowa laws regarding this issue. However, we hope to be able to offer this option to our patients in the near future.

Adoption

Process

Adoption is an option that can be considered by anyone seeking parenthood. It can be domestic or internation and open or closed. Open adoption refers to a process in which the birthmother is known to you and you to her. The possibility for contact before and after the birth is possible. Closed adoptions are private in that you and the birthmother will have limited information about one another and no information about one another's identities. You also may consider foster care, with the future possibility of adoption through that process. Regardless of which route you take, the state in which you live will have laws that regulate adoption. In most cases you will have contact with state-certified social workers who will assist you in the process. Adoption agencies may be private, not-for-profit organizations, such as Jewish Family and Children's Services or Catholic Charities. They may be local or state government bodies such as county child welfare service agencies. There also are for-profit organizations and lawyers that specialize in coordinating domestic and/or international adoptions. Most adoption agencies report that they do not rule out cancer survivors as potential parents, especially with documentation from a doctor stating that lifespan and quality of life are expected to be good. However, some agencies do require a certain amount of time to pass before allowing a survivor to be eligible (e.g. 5 years). The adoption process takes time (6 months to 2 or 3 years) and costs vary greatly, from $2,500 to $35,000.

THE NEXT STEP

Deciding if fertility preservation is right for you

If you are at risk for infertility from your cancer treatment, it is important to think about the significance of parenting to you. Questions you may want to ask yourself include:

- Have I always wanted children?
- Would I prefer adoption to other parenthood options?
- Does it matter to me if my children are biologically related to me?
- Am I open to using donor sperm or donor embryos?
- How many children do I want to have?
- How does my partner/spouse feel about all of these issues?
- Do I have ethical or religious concerns about assisted reproductive technologies?

If you think you may want to pursue fertility preservation, start with a discussion with your oncologist. Questions you may want to ask him or her include:

- How will my diagnosis and treatment affect my fertility?
- Are there alternative cancer treatments with fewer side effects on my fertility?
- Can I safely delay my treatment to undergo a fertility preservation procedure?
- Is it safe for me to use fertility drugs? (Is my cancer sensitive to hormones?)
- Is pregnancy safe for me? How long should I wait before I try to get pregnant?

Scheduling an appointment

Your oncologist can help direct you to the appropriate clinic, but you will likely have an appointment in our IVF or Endocrine clinic. The number to contact that clinic is 319-356-8483.

Labs and testing that can be done prior to your appointment

Blood tests for HIV, Hepatitis (B surface antigen and C antibody) and RPR (Syphilis) are required for both partners undergoing IVF. These should be ordered by your local physician and results may be mailed or faxed to us or hand carried to your preliminary appointment. Use of any donor gametes here at UIHC requires pretreatment counseling by a Health Psychologist. Call the clinic to discuss your particular circumstances prior to getting these tests done.

THE UIHC IVF TEAM

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- Kathy Koehler, RN
- Shirley Hoeppner, RN

IVF Operating Room Technician

- Patricia Spevacek

Program Associate

- Pam Funke

Receptionist Secretarial Support

- Cheryl Cullers-Hoard

OTHER RESOURCES

Fertile Hope
Founded in 2001 by Lindsay Beck, Fertile Hope is a national nonprofit organization headquartered in New York City, dedicated to providing reproductive information, support and hope to cancer patients and survivors whose medical treatments present the risk of infertility. Provides information for patients and physicians, including financial assistance options, support, and ongoing clinical trials.
www.fertilehope.org

Association of Cancer Online Resources
A nonprofit organization based in NYC. Subscribe to a cancer/infertility related internet mailing list at http://listserv.acor.org/archives/cancer-fertility.html
www.acor.org

Live Strong, the Lance Armstrong Foundation
Founded in 1997 by cancer survivor and champion cyclist Lance Armstrong, the LAF is a registered nonprofit organization located in Austin, Texas, created to inspire and empower people affected by cancer.
www.livestrong.org

Cryogenic Laboratories, Inc.
This cryobank was established in the 1970's as the country's first private sperm bank. Along with an extensive donor sperm program, CLI offers a convenient "Priority Male" service, which allows men to collect specimens at home and have them shipped overnight to their cryobank for storage.
1800-466-2796. info@cryolab.com
www.cryolab.com

100 Questions & Answers About Cancer & Fertility
Kutluk H. Oktay, MD,
Written by an ObGyn/reproductive medicine specialist and cancer/fertility patient advocate, with commentary from actual patients, this is an invaluable resource for anyone struggling with the medical, physical, and emotional turmoil of cancer and infertility.