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fertileHOPE

fertility resources for cancer patients

Cancer & Fertility

Fast Facts for Reproductive Professionals

information • support • hope

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introduction

Each year, approximately 140,000 Americans under the age of 45 are diagnosed with cancer. Cancer survival rates are higher than they have ever been, and patients under the age of 45 now have a 77% survival rate. Simultaneously, there are more fertility preservation options than ever before. So, while cancer treatments can be permanently sterilizing, the reproductive community is providing great hope for parenthood after cancer.

As evidenced by the May 1, 2006 release of the American Society of Clinical Oncology's (ASCO) Recommendations on Fertility Preservation in Cancer Patients, the cancer community is providing improved information about the reproductive risks associated with cancer treatments. As a result, the reproductive community will continue to see more cancer patients who have fertility concerns. To read the complete guideline, please go to www.asco.org.

Often challenging, however, is meeting the unique needs of cancer patients through your practice's existing operational infrastructure. Accordingly, the purpose of this booklet is to provide an overview of cancer-related infertility as well as to provide guidance on how to effectively meet the unique reproductive needs of cancer patients and survivors.

role of the reproductive professional

As a fertility specialist, you will primarily see two types of cancer patients: newly diagnosed patients and long-term survivors. Newly diagnosed patients will be seeking your assistance with fertility preservation before the initiation of potentially sterilizing cancer treatment. Cancer survivors may need your assistance in order to have a child. The needs of these patients are distinct from those of your standard infertility patients in a few ways and, therefore, a modification of your standard practices may be necessary.

- **Patients are coping with diagnosis of a life-threatening disease**
  Newly diagnosed cancer patients are likely dealing with significant shock and emotional distress inherent to their cancer diagnosis. Digesting the "double blow" of cancer and possible infertility is especially traumatic and will probably require increased sensitivity.

- **Shortened "window of opportunity" for treatment**
  The cancer patient, generally, will have a short period of time in which he or she will be able to undergo fertility preservation techniques. Time is of the essence. For example, many patients have a hiatus of only two to six weeks between surgery and adjuvant therapy, which can be a good time for fertility preservation. Others may have even less time, and may not, therefore, be eligible for standard fertility procedures. Patients, especially female patients, must be triaged and counseled in an expedited fashion in order to afford them their full range of fertility preservation options.

- **Consent procedures**
  While informed consent for disposition of embryos, gametes and tissues must be obtained from all patients, cancer patients are presenting with a life-threatening condition, so this discussion is particularly salient. In addition, special consent forms and processes may need to be developed for patients who are participating in experimental procedures or for pediatric patients.

- **Need for efficient, prospective family planning**

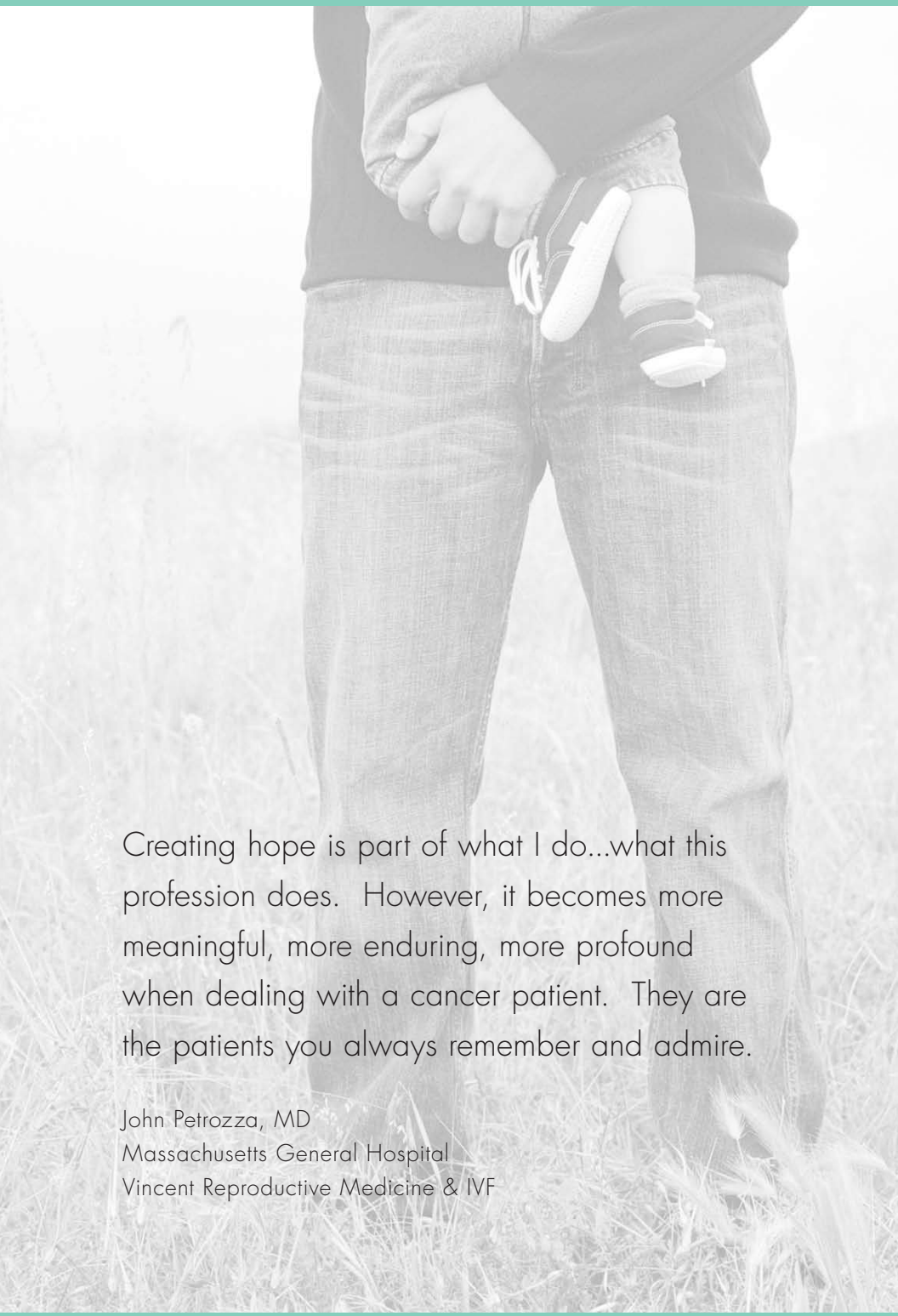
  Cancer patients may become sterile immediately after treatment. Therefore, whatever amount of tissue and/or gametes that can be preserved prior to cancer treatment may represent the patient's only reserve of genetic material. Patients need to understand this situation both when selecting a fertility preservation option and when they return to use the stored tissue. For example, a typical patient might want to use IUI with deposited sperm, to keeps costs down. However, for an azoospermic man with a limited amount of sperm, IVF with ICSI might represent a more efficient, less wasteful approach. Similarly, a single female patient who may have time to undergo only one cycle before cancer treatment might consider using donor sperm to create embryos in order to increase her chances of a later pregnancy, whereas a patient with time to undergo multiple cycles might decide to freeze eggs even though the procedure is currently less efficient. These considerations differ significantly from those facing standard infertility patients who have the freedom to undergo multiple cycles and sample different options over time.

- **Medical considerations in addition to fertility**

  In addition to standard assessment of the patient's suitability for any fertility procedure, you are highly encouraged to have an open dialogue with the patient's oncologist. This is true for both newly diagnosed patients who may have hormonally-sensitive cancers and other medical contra-indications due to acute illness, as well as for survivors who may have on-going health or pregnancy concerns.

- **Designation of a cancer contact**

  Because of the differing concerns detailed above, it may be helpful for you to designate at least one person on staff to serve as an expert in understanding, assessing and addressing the needs of this specific patient population.



Creating hope is part of what I do...what this profession does. However, it becomes more meaningful, more enduring, more profound when dealing with a cancer patient. They are the patients you always remember and admire.

John Petrozza, MD
Massachusetts General Hospital
Vincent Reproductive Medicine & IVF

men

risks

Cancer itself may be correlated with low sperm counts, as has been demonstrated in men with Hodgkin lymphoma and testicular cancer. The primary threat for male patients, however, is compromised sperm production, quality, motility and DNA damage caused by exposure to **chemotherapy** and/or **radiation**. Because reproductive damage is generally caused by cancer treatment, patients with almost any type of cancer may be at risk. Factors determining the likelihood of reproductive damage 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). **Surgery** to reproductive organs such as the testes affect fertility, and pelvic surgery can cause nerve damage that may interfere with ejaculation.

To better understand the level of risk associated with various cancer treatments, please consult the chart on page 6.

risk of azoospermia

from chemotherapy and radiation treatments for cancer

This table represents a compilation of clinical experience and current research on common cancer treatments that may impact reproductive function in men.

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

options

The most proven and successful method of **fertility preservation** for men is **sperm banking**. The benefit of sperm banking for patients with **low sperm count** and/or quality has been greatly enhanced by the development of **ICSI** (intracytoplasmic sperm injection).

Post-treatment, patients should undergo **semen analysis** to assess their reproductive status. Patients who remain **azoospermic**, may consider techniques such as **testicular sperm extraction**. For those patients who suffer nerve damage as a result of their cancer treatment, and are unable to ejaculate, techniques for stimulation or electroejaculation may be useful. Options such as **donor sperm** and **adoption** can also be presented as a means of fatherhood.

Aside from hereditary genetic syndromes, there is no evidence that a history of cancer or cancer treatment increases the risk of cancer or congenital abnormalities in the progeny of survivors.

Please see the chart on pages 8 and 9 for more detail on the available reproductive options for men, including experimental procedures.

male reproductive options

OPTION	**Sperm Banking** (Masturbation)	**Sperm Banking** (Alternative Collection Methods)	**Radiation Shielding of Gonads**
MEDICAL STATUS	Standard	Experimental	Standard
DEFINITION	Sperm is obtained through masturbation, then frozen	Sperm obtained through testicular extraction or electroejaculation under sedation	Use of shielding to reduce the dose of radiation delivered to the testes
PUBERTAL STATUS	After puberty	After puberty	Before and after puberty
TIME REQUIREMENT	Outpatient procedure	Outpatient procedures	In conjunction with radiation treatments
SUCCESS RATES	Generally high The most established technique for men	If sperm is obtained, similar to standard sperm banking	Possible with select radiation fields and anatomy
COST	Approx. $1,500 for 3 samples; storage fees average $500/year	Varies greatly based on collection method	Generally included in the cost of radiation treatments
TIMING	Before treatment	Before treatment	During treatment
SPECIAL CONSIDERATIONS	Deposits can be made every 24 hours	Can be considered if male cannot ejaculate	Expertise required; does not protect against effects of chemotherapy

male reproductive options

	Testicular Tissue Freezing	Testicular Sperm Extraction	Donor Sperm	Adoption
	Experimental	Standard	Standard	Standard
	Tissue obtained through biopsy and frozen for future use	Use of biopsy to obtain individual sperm from testicular tissue	Sperm donated by a man for artificial insemination or IVF	Process that creates a legal parent-child relationship
	Before and after puberty	After puberty	After puberty	After puberty
	Outpatient procedure	Outpatient procedure	Readily available for purchase	Varies depending on the type of adoption
	No available human success rates	30-70% in post-pubescent patients	50-80%	N/A
	$500-$2,500 for surgery; $300-$1,000 for freezing; $500/year for storage	$4,000-$16,000 (in addition to costs for IVF)	$200-$500 per vial (in addition to costs for IUI or IVF)	$2,500-$35,000
	Before treatment	Before or after treatment	After treatment	After treatment
	May be only option for pre-pubescent boys	Center should be able to freeze sperm found at time of biopsy	Can choose donor based on wide range of characteristics	Medical history often a factor

women

risks

While cancer itself does not appear to affect fertility in women, cancer treatments pose a variety of reproductive risks including **immediate infertility**, **premature menopause**, and **compromised ability to carry a pregnancy** due to uterine or cervical damage. Factors determining the likelihood of reproductive damage include: drug type and dosage; radiation location and dosage; patient's age and pubertal status at the time of treatment; and pre-treatment fertility (which is often unknown).

Chemotherapy and **radiation** can damage or destroy oocytes and follicles, which can cause either immediate **menopause** or **premature menopause** years after treatment. Many patients who return to menstruation after the completion of treatment believe their reproductive capacity has not been affected. The possibility of premature menopause should be discussed with these patients. In addition to oocyte damage, new research shows that chemotherapy and radiation may also affect ovarian blood vessels and stromal function.

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. **Radiation** can damage the uterus and increase the risk of **miscarriage** or **low birth-weight**. Survivors who received pelvic radiation may be advised to consider consulting a high-risk obstetrician before becoming pregnant.

To better understand the level of risk associated with various cancer treatments, please consult the chart on page 7.

risk of amenorrhea from chemotherapy and radiation treatments for cancer

The following table represents a compilation of both clinical experience and the published research on the impact of common cancer treatments on menstruation. Generally, studies have not focused on other measures of reproductive capacity, such as hormone levels or follicle counts which may more accurately reflect reproductive capacity.

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	Wilms' tumor, neuroblastoma, sarcoma, Hodgkin lymphoma
	TBI radiation doses	Bone marrow transplant/stem cell transplant (BMT/SCT)
	CMF, CEF, CAF x 6 cycles in women 40 +	Breast cancer
	Cyclophosphamide 5 g/m^2 in women 40+	Multiple cancers
	Cyclophosphamide 7.5 g/m^2 in girls < 20	Non-Hodgkin lymphoma (NHL), neuroblastoma, acute lymphoblastic leukemia (ALL), sarcoma
	Alkylating chemotherapy (e.g., cyclophosphamide, busulfan, melaphan) conditioning for transplant	BMT/SCT
	Any alkylating agent (e.g., cyclophosphamide, ifofsamide, busulfan, BCNU, CCNU) + TBI or pelvic radiation	BMT/SCT, ovarian cancer, sarcoma, neuroblastoma, Hodgkin lymphoma
	Protocols containing procarbazine: MOPP, MVPP, COPP, ChIVPP, ChIVPP/EVA, BEACOPP, MOPP/ABVD, COPP/ABVD	Hodgkin lymphoma
	Cranial/brain radiation ≥40 Gy	Brain tumor
Inter-mediate Risk ~30-70% of women develop amenorrhea post-treatment	CMF 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	Wilms' tumor, neuroblastoma
	Spinal radiation ≥25 Gy	Spinal tumor, brain tumor, neuroblastoma, relapsed ALL or NHL
Low Risk <20% of women develop amenorrhea post-treatment	AC in women 30-39	Breast cancer
	CMF, CEF, or CAF x 6 cycles in women under 30	Breast cancer
	Non-alkylating chemotherapy: ABVD, CHOP, COP	Hodgkin lymphoma, NHL
	AC (anthracycline, cytarabine)	Acute myeloid leukemia (AML)
	Multi-agent therapies	ALL
Very Low/ No Risk Negligible effect on menses	MF (methotrexate, 5-FU)	Breast cancer
	Vincristine (used in multi-agent therapies)	Leukemia, Hodgkin lymphoma, NHL, neuro-blastoma, 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)

options

The most proven and successful method of **fertility preservation** for women is **embryo freezing**. "Emergency IVF" – or a shortened controlled cycle – may have to be implemented to fit into the patient's cancer treatment timeline. Cancer patients who have concerns about using IVF hormones, are single, or do not have time to undergo standard IVF to create embryos may want to look into experimental options.*

For women with hormone-sensitive tumors who do not want to undergo ovarian stimulation with standard IVF medications, protocols using alternative medications such as tamoxifen and aromatase inhibitors to limit hormone exposure may be considered.

Patients who are single or do not have a male partner to provide sperm for the creation of embryos may want to think about **egg freezing.***

Patients who do not have time for ovarian stimulation may also want to consider experimental options such as **in vitro maturation*** or **ovarian tissue freezing***, procedures that can be performed fairly quickly. In vitro maturation involves removing immature oocytes and then maturing them in vitro. Once matured, the oocytes can either be frozen or fertilized to create embryos and then frozen. Ovarian tissue freezing involves the removal, sectioning and freezing of an ovary. The ovarian strips can be transplanted later to restore hormonal function and for use with IVF.

Post-treatment, patients should undergo **fertility testing** to assess their reproductive status. Patients should not rely on the return of menses as an indication of fertility, and the risk of early menopause should be thoroughly discussed. Patients who either are at high risk of premature menopause or show signs of reduced fertility may want to consider fertility preservation after cancer treatment if they are not ready to start a family before menopause is likely to occur.

For those patients who are **infertile** or who are **unable to carry a pregnancy**, options such as **donor eggs**, **donor embryos**, **surrogacy** and **adoption** should also be presented as a means of motherhood. While data is limited, pregnancy after cancer does not appear to cause recurrence, even in patients who have hormonally sensitive tumors.

In addition, aside from hereditary genetic syndromes and in utero exposure to chemotherapy, there is no evidence that a history of cancer, cancer therapy, or fertility interventions increase the risk of cancer or congenital abnormalities in the progeny of survivors.

Please see the chart on pages 10-11 for more detail on the available reproductive options for women, including experimental procedures.

*The American Society for Reproductive Medicing (ASRM) recommends that all experimental procedures be offered under IRB protocol.

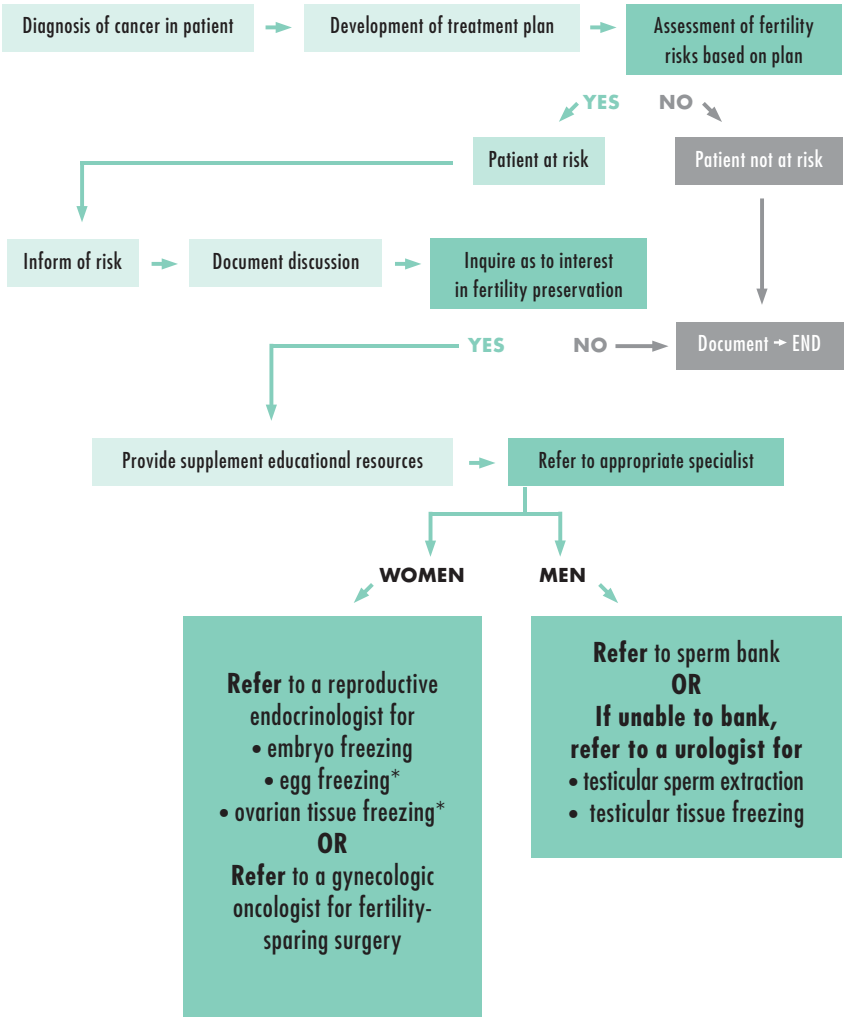
female reproductive options

OPTION	Embryo Freezing	Egg Freezing	Ovarian Tissue Freezing	In Vitro Maturation	Radiation Shielding of Gonads	Ovarian Transposition
MEDICAL STATUS	Standard	Experimental	Experimental	Experimental	Standard	Standard
DEFINITION	Harvesting eggs, in vitro fertilization and freezing of embryos for later implantation	Harvesting and freezing of unfertilized eggs	Freezing of ovarian tissue and reimplantation after cancer treatment	Harvesting immature eggs and maturing them in the laboratory	Use of shielding to reduce scatter radiation to the reproductive organs	Surgical repositioning of ovaries away from the radiation field
PUBERTAL STATUS	After puberty	After puberty	Before or after puberty	After puberty	Before or after puberty	Before or after puberty
TIME REQUIREMENT	10-14 days from menses Outpatient surgical procedure	10-14 days from menses Outpatient surgical procedure	Outpatient surgical procedure	2-10 days Outpatient surgical procedure	In conjunction with radiation treatments	Outpatient procedure
SUCCESS RATES	Approximately 20-33% per transfer; varies by age & center Thousands of babies born	Approximately 21.6% per embryo transfer 500+ live births	Case reports of two live births	Up to 30% per embryo transfer	Only possible with selected radiation fields and anatomy	Approximately 50% due to altered blood flow and scattered radiation
COST	Approximately $12,000/cycle; storage fees & pregnancy costs additional	Approximately $12,000/cycle; storage fees & pregnancy costs additional	$12,000 for procedure; storage fees & reimplantation costs additional	Approximately $5,000	Generally included in cost of radiation	Unknown; may be covered by insurance
TIMING	Before treatment	Before treatment	Before treatment	Before treatment	During treatment	Before treatment
SPECIAL CONSIDERATIONS	Need partner or donor sperm	May be attractive to single women or those opposed to embryo creation	Not suitable if high risk of ovarian metastases Only preservation option for pre-pubescent girls	Does not require standard ovarian stimulation Only a few centers offer this technique	Expertise required Does not protect against effects of chemotherapy	Expertise required

female reproductive options

	Radical Trachelectomy	Ovarian Suppression	Donor Embryos	Donor Eggs	Gestational Surrogacy	Adoption
	Standard	Experimental	Standard	Standard	Standard	Standard
	Surgical removal of the cervix with preservation of the uterus	Medication used to suppress ovarian cycling	Embryos donated by a couple	Eggs donated by a woman	Woman carries a pregnancy for another woman or couple	Process that creates a legal parent-child relationship
	After puberty	After puberty	After puberty	After puberty	After puberty	After puberty
	Inpatient surgical procedure	In conjunction with chemotherapy	Varies; is done in conjunction with IVF	Varies; is done in conjunction with IVF	Varies; time is required to find surrogate and implant embryos	Varies depending on type of adoption
	No evidence of higher cancer recurrence rates in appropriate candidates	Unknown; conflicting results reported Larger randomized trials in progress	Unknown; higher than that of frozen embryo IVF transfers	40-50%	Similar to IVF–approximately 30%	N/A
	Generally included in the cost of cancer treatment	$500/month	$5,000-$7,000 (in addition to costs for IVF)	$5,000-$15,000 (in addition to costs for IVF)	$10,000-$100,000	$2,500-$35,000
	During treatment	During treatment	After treatment	After treatment	After treatment	After treatment
	Limited to early stage cervical cancer Offered at a limited number of centers	Does not protect from radiation effects	Donor embryo available through IVF clinics or private agencies	Patient can choose donor based on various characteristics	Legal status varies by state	Medical history often a factor

advising your patient



*ASRM recommends that all experimental procedures be offered under IRB protocol.

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about schering-plough

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contact us

Fertile Hope is a national, nonprofit organization dedicated to providing reproductive information, support and hope to cancer patients whose medical treatments present the risk of infertility.

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