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Cancer & Fertility

Fast Facts for Oncology Professionals



information • support • hope

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introduction

Each year, approximately 140,000 Americans under the age of 45 are diagnosed with cancer. Most of these patients face good prospects for survival, but many are at risk for permanent infertility as a result of their treatments. Advances in both fertility preservation and infertility treatments are occurring at a rapid rate and there are now viable options available for your patients.

Major cancer organizations including the President's Cancer Panel and the National Cancer Institute have recognized that, as survivorship increases, the need to address the long-term consequences of cancer treatment, including infertility, also increases. As a result, on May 1, 2006, the American Society of Clinical Oncology (ASCO) released the first guideline on fertility preservation for people with cancer. For the complete guideline, please go to www.asco.org.

This brochure is designed to highlight the recommendations of the ASCO guideline, and to give you some background information about cancer-related infertility. While patients' risks for infertility and their options for preservation differ, all patients need to understand the effects of cancer treatment on their reproductive health before beginning a course of treatment. Please use this information to initiate a meaningful discussion with your patients, so that they can make the parenthood decisions that are right for them.



men risks

Cancer itself can 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 affects 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 3.

options

The most proven and successful method of **fertility preservation** for men is **sperm banking**. The benefit for patients with **low sperm count** and/or quality has been greatly enhanced by the development of **ICSI** (intracytoplasmic sperm injection), which allows a single sperm to be used to fertilize an egg.

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 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 4 and 5 for more detail on the available reproductive options for men, including experimental procedures.

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) Testicular radiation dose > 2.5 Gy in men Testicular radiation dose \geq 6 Gy in boys Protocols containing procarbazine: COPP, MOPP, MVPP, ChIVPP, ChIVPP/EVA, MOPP/ABVD, COPP/ABVD Alkylating chemotherapy for transplant conditioning (cyclophosphamide, busulfan, melphalan) Any alkylating agent (e.g., procarbazine, nitrogen mustard, cyclophosphamide) + TBI, pelvic radiation, or testicular radiation Cyclophosphamide >7.5 g/m ² Cranial/brain radiation \geq 40 Gy	Bone marrow transplant/stem cell transplant(BMT/SCT) Testicular cancer, acute lymphoblastic leukemia (ALL), non-Hodgkin lymphoma (NHL) ALL, NHL, 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 \leq 2g/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 post-treatment	Non-alkylating chemotherapy: ABVD, OEPA, NOVP, CHOP, COP Testicular radiation dose 0.2 – 0.7 Gy	Hodgkin lymphoma, NHL Testicular cancer
Very Low/ No Risk No effects on sperm production	Testicular radiation dose < 0.2 Gy Interferon- α Radioactive iodine	Multiple cancers Multiple cancers Thyroid
Unknown Risk	Irinotecan Bevacizumab (Avastin) Cetuximab (Erbix) 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)

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 Whole abdominal or pelvic radiation doses ≥ 15 Gy in pre-pubertal girls ≥ 10 Gy in post-pubertal girls TBI radiation doses CMF, CEF, CAF x 6 cycles in women 40 + Cyclophosphamide 5 g/m ² in women 40+ Cyclophosphamide 7.5 g/m ² in girls < 20 Alkylating chemotherapy (e.g., cyclophosphamide, busulfan, melaphan) conditioning for transplant Any alkylating agent (e.g., cyclophosphamide, ifosfamide, busulfan, BCNU, CCNU) + TBI or pelvic radiation Protocols containing procarbazine: MOPP, MVPP, COPP, ChiVPP, ChiVPP/EVA, BEACOPP, MOPP/ABVD, COPP/ABVD Cranial/brain radiation ≥ 40 Gy	Multiple cancers Wilms' tumor, neuroblastoma, sarcoma, Hodgkin lymphoma Bone marrow transplant/stem cell transplant (BMT/SCT) Breast cancer Multiple cancers Non-Hodgkin lymphoma (NHL), neuroblastoma, acute lymphoblastic leukemia (ALL), sarcoma BMT/SCT BMT/SCT, ovarian cancer, sarcoma, neuroblastoma, Hodgkin lymphoma Hodgkin lymphoma 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 AC in women 40+ Whole abdominal or pelvic radiation 10-<15 Gy in prepubertal girls Whole abdominal or pelvic radiation 5-<10 Gy in postpubertal girls Spinal radiation ≥ 25 Gy	Breast cancer Breast cancer Wilms' tumor Wilms' tumor, neuroblastoma Spinal tumor, brain tumor, neuroblastoma, relapsed ALL or NHL
Low Risk <20% of women develop amenorrhea post-treatment	AC in women 30-39 CMF, CEF, or CAF x 6 cycles in women under 30 Non-alkylating chemotherapy: ABVD, CHOP, COP AC (anthracycline, cytarabine) Multi-agent therapies	Breast cancer Breast cancer Hodgkin lymphoma, NHL Acute myeloid leukemia (AML) ALL
Very Low/ No Risk Negligible effect on menses	MF (methotrexate, 5-FU) Vincristine (used in multi-agent therapies) Radioactive Iodine	Breast cancer Leukemia, Hodgkin lymphoma, NHL, neuroblastoma, rhabdomyosarcoma, Wilms' tumor, Kaposi's sarcoma Thyroid cancer
Unknown Risk	Paclitaxel, docetaxel (Taxanes used in AC protocols) Oxaliplatin Irinotecan Bevacizumab (Avastin) Cetuximab (Erbix) Trastuzumab (Herceptin) Erlotinib (Tarceva) Imatinib (Gleevec)	Breast cancer Ovarian cancer Colon cancer Colon, non-small cell lung Colon, head & neck Breast cancer Non-small cell lung, pancreatic 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 Medicine (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

value of fertility to patients and survivors

Although patients may not know to bring up the topic of infertility, evidence to date suggests that it is important to them:

- Fertility preservation is of great significance to many people diagnosed with cancer
- Banking sperm was a positive factor in coping emotionally with cancer, even if samples were never used
- Although cancer survivors can become parents through options such as adoption and third-party reproduction, most prefer to have biological offspring
- There is an increased risk of emotional distress in those who become infertile because of their cancer treatments

role of the oncology professional

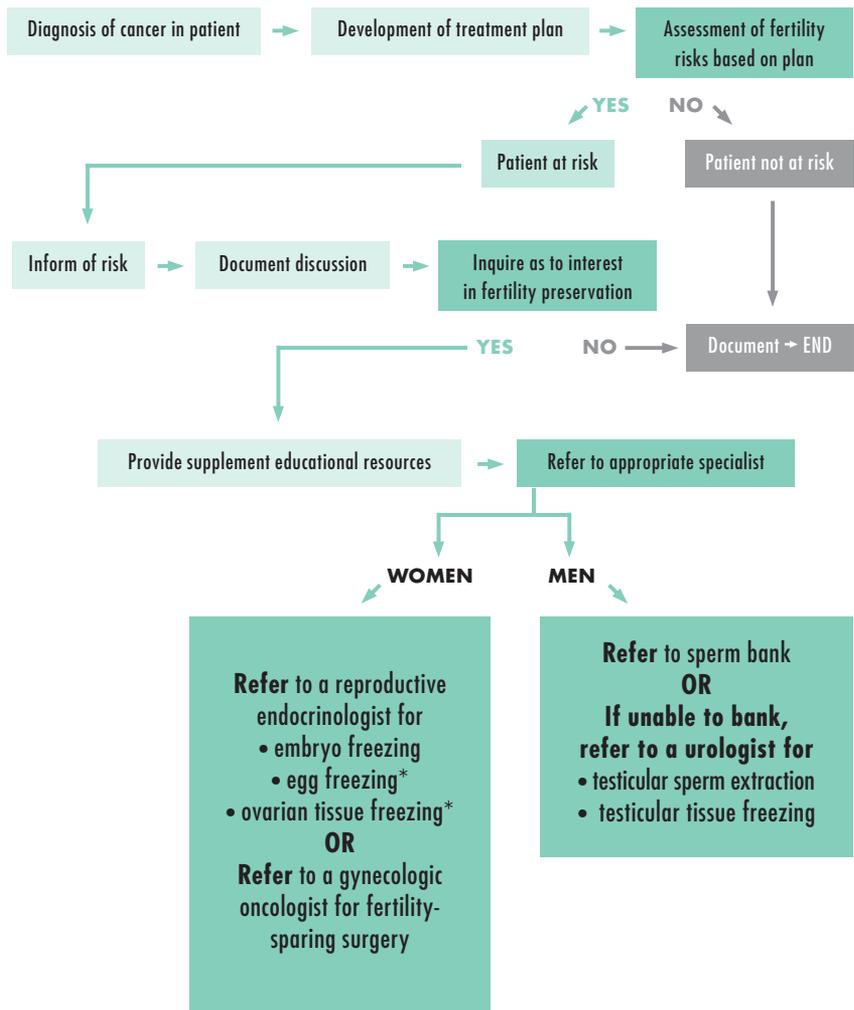
As outlined by ASCO's fertility preservation guideline, oncology healthcare professionals should implement the following as part of the education and informed consent process prior to initiating cancer therapies:

- Discuss infertility as a potential risk of therapy as early in treatment planning as possible with patients treated during their reproductive years
- Be prepared to discuss possible fertility preservation options
- Refer patients to appropriate reproductive specialists and psychosocial providers
- Answer basic questions about whether fertility preservation options decrease the chance of successful cancer treatment, increase the risk of maternal or perinatal complications, or compromise the health of offspring

"No one should be deprived of one of the most joyous experiences in life because they didn't get available information at a critical time."

Heidi, 39, Ewing's Sarcoma

advising your patient



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

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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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fertility resources for cancer patients

P.O. Box 624 New York, NY 10014
888 994.HOPE tel 212 242.4570 fax www.fertilehope.org