

Melanoma-What Every Woman Need to Know about Fertility and Pregnancy

Women diagnosed with melanoma may require counseling for fertility preservation, fertility treatment and safety of pregnancy after treatment. Melanoma is one of the most common cancers in young adults in the United States. In the US and



worldwide, there is dramatic increase in the incidence of skin melanomas. Approximately 30,000 women are expected to be diagnosed with melanoma in 2010, one third will be in their reproductive years. Its the most common cancer in young adults 25 to 29 year old. Its more common in white women compared to African Americans and

Hispanics. Approximately 10% of melanomas run in families or are genetically inherited. Treatment of melanoma requires surgery. In advanced melanoma, chemotherapy is added. Dacarbazine-DTIC is an alkylating agent used for treating melanomas. Immune therapy is also used for advanced melanomas- interferon α or IL-2.

In early stages, surgery is the only required treatment. In advanced stages if chemotherapy is used, [ovarian reserve](#) may be diminished and this may reduce woman's ability to get pregnant. The use of immune therapy is not known to affect future fertility. The effects of newer targeted therapies and vaccines on fertility are also unknown.

Melanoma and fertility treatment. The estrogen receptors were

found on melanoma cells. Some researchers detected no significant increase in the risk of melanoma after treatment with fertility drugs, except possibly slight increase in risk in women who delivered children before. The relationship between



estrogen exposure and melanoma is controversial. Women seeking fertility preservation before exposure to chemotherapy or melanoma survivors desiring pregnancy after completing treatment should consult with a fertility preservation specialist about the risks and benefits of fertility treatment and the safety of pregnancy. The ovarian stimulation regimen can also be modified to minimize estrogen exposure. It may also be possible for women with inherited predisposition to melanoma to avoid transmission to future children through testing of embryos-PGD.

Melanoma and pregnancy. Ten studies including 5600 women found that pregnancy does not reduce survival in women diagnosed with melanoma. Women treated for melanoma who subsequently became pregnant were not adversely affected compared to women who did not get pregnant after treatment. For thin tumors- <1.5mm most experts do not recommend deferring pregnancy. For thicker tumors, physicians may recommend deferring pregnancy for two years as most recurrences take place during that interval. Read more at <http://nycivf.org>



What Does Borderline Ovarian Tumor Mean to Your Fertility?

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Fertility in women diagnosed with borderline ovarian tumors can be reduced or lost due to surgical treatment. Counseling regarding fertility preservation shortly after diagnosis can increase the chance of pregnancy following treatment.

Borderline-low malignant potential ❑ ovarian tumors

The cells in borderline tumors, proliferate more than benign ovarian cysts but less than frank malignant ovarian tumors. Multiple layers of these cells are seen on pathology slides, but they do not invade surrounding tissues as in malignant tumors. They are diagnosed in approximately 4000 of women each year in the US and are more commonly encountered in reproductive age women. These tumors are usually cystic, sometimes with surrounding implants. Low malignant potential tumors are treated surgically (removal of cyst, removal of the ovary or sometimes removal of both ovaries and the uterus). They generally do not require chemotherapy for treatment. The majority of these tumors are associated with very high survival (10 year survival >90% in stage I and II), although some may recur or turn malignant.

There is no difference in survival if borderline tumors were treated with removal of the cyst, removal of the ovary or removal of the uterus and both ovaries. Recurrence may be lower after hysterectomy (5%) compared to salpingoophorectomy (15%) and cyst excision (30%). The high rate for recurrence

after conservative surgery indicates the need for strict and long term follow up (pelvic exams, ultrasound and tumor markers). Some recurrences take place years after initial surgery and are sometimes malignant.

Fertility risks in women diagnosed with borderline tumors

Fertility risks in women diagnosed with low malignant potential ovarian tumors include loss of ovarian tissue and pelvic scarring that can block the fallopian tubes especially if open approach is used for treatment compared to laparoscopy (minimal access surgery). Some loss of ovarian tissue does occur even during cyst removal from the ovary. Ovarian reserve can be tested after surgery using transvaginal ultrasound evaluation for ovarian volume and number of antral follicles. Ovarian function can also be assessed using day 2 FSH and estradiol levels and antimullerian hormone (AMH).

Fertility preservation strategies in women diagnosed with borderline ovarian tumors

1. Conservative surgery

Ovarian cystectomy can be considered in reproductive age women, especially in early disease with favorable pathology and absence of implants. Recurrence is relatively high but can be managed with repeat excision if not malignant. If pregnancy is desired following surgery, fertility factors; ovulation, fallopian tubes and sperm factors should be investigated and treated accordingly

2. Embryo and oocyte cryopreservation

Women at risk for diminished fertility due to surgery, especially if requiring removal of the ovaries or repeat

excision of cyst, can consider ovarian stimulation, egg retrieval and egg freezing or IVF and embryo freezing. There is no evidence that ovarian stimulation and exposure to high estrogen increases the risk for recurrence. It is not clear if border line cells are sensitive to estrogen increase during ovarian stimulation. Two options are available to reduce estrogen exposure: to perform IVF in a natural cycle (low egg yield) or to modify the stimulation protocol, through adding an aromatase inhibitor, similar to that used for breast cancer. Alternatively, short stimulation followed by retrieval of immature eggs followed by in vitro maturation can be performed.

Women diagnosed with borderline ovarian tumors are at risk for diminished fertility because of surgical treatment(s). This is especially true if repeat surgical excision is required. Collaboration between a gynecologic oncologist and a reproductive endocrinologist enable adequate surgical treatment, strict follow up and preservation of future fertility in reproductive age women.

[Egg Freezing what Do you Hope to Accomplish?](#)

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The best approach motherhood is to actually try to get pregnant. Though methods of fertility preservation are very helpful, none is a guarantee to make a baby in the future. So

the primary advice is “try to get pregnant if you can” after checking different fertility factors (male, tubal and ovarian factors as well preconception screening). If getting pregnant is not feasible in the short term, due to medical or social issues, egg freezing is considered. *A reproductive endocrinologist is faced with the challenge of foreseeing if a specific woman, when stimulated and her eggs are harvested and frozen, has a reasonable potential to conceive using these eggs at one time in the future.*

Indication for Egg Freezing

Women should consider [egg freezing](#) when specific medical or age related situations threatens their ability to have a child in the future.

1. Fertility preservation: When a medical disorder or its treatment can diminish ovarian reserve and reduce the chance for conception e.g cancer treatment (most common is breast cancer), lupus nephritis requiring treatment with chemotherapy, blood diseases requiring bone marrow transplantation, premature ovarian dysfunction and others. About 2 weeks should be available for an egg freezing cycle.
2. Fertility extension (no male partner): women with no male partner and declining the use of donor sperm can freeze their eggs to use in the future when in a committed relationship.
3. Fertility extension (with a male partner): women with a male partner can elect to freeze some of their eggs unfertilized. Unfertilized eggs are under the control of the woman alone, unlike embryos that cannot be used without the consent of both partners.
4. IVF with failed sperm retrieval or ejaculation: In some cases with male factor with failed retrieval of sperm from the testes or failed ejaculation, eggs can be frozen and used later when sperm are available.

5. Children undergoing treatment for cancer and other diseases with the ascent of their parents.

What should you consider before proceeding to egg freezing

i. Women <38 years with good ovarian reserve: are excellent candidates for egg freezing. Good reserve is indicated by antral follicle count >10 as seen on vaginal ultrasound and AMH levels > 1.75 ng/mL. They will likely produce a good number of oocytes to freeze in a single cycle. These eggs are relatively healthy as they are young. Age <36 years was the best predictor of egg freezing so far in scientific reports.

ii. Women <38 years with diminished ovarian reserve: are still good candidates for egg freezing. They produce lower number of eggs after stimulation but their oocytes are relatively healthy (chromosomally normal). They can undergo more than one cycle of egg freezing if the first cycle yields <8 mature eggs.

iii. Women 38-40 years with good reserve: can still consider egg freezing with no further delay.

vi. Women 38-40 years with diminished ovarian reserve: should consider egg freezing with caution. They will not produce a good number of eggs and may require multiple cycles of egg freezing.

V. Women >41y are not good candidates for egg freezing even if they have a good reserve as the majority of their oocytes are not chromosomally normal. Although pregnancies were reported from vitrified oocytes up to age 44, the chance of pregnancy is quite low in women older than 40.

Realistic Expectations for egg freezing

Not only should the number and quality of eggs be considered, but also the survival of thawed eggs, fertilization and

ultimate ability to implant. These issues are very sensitive to the method of ovarian freezing. Vitrification (rapid freezing) is not the method of choice for low temperature storage of eggs due to high survival and subsequently fertilization and embryo development ([more details here](#) and [here](#)).

Survival on average 85% of vitrified thawed eggs survive, irrespective of age.

Fertilization approximately 80% of thawed eggs fertilize after injecting each with a sperm (ICSI).

Age specific chance for a live birth after thawing of vitrified eggs can be presented in different ways. The delivery rate is approximately 5 to 15% per thawed egg depending upon the female age at freezing. For example, if eggs are thawed and fertilized and three embryos were transferred to the uterus, the probability of delivery would be 25% at age 30 and 15% at age 40.

If a 35 year old decided to proceed with an egg freezing cycle and produced 10 eggs, 8 eggs were mature and frozen. When she present back 10 years later to utilize her eggs and thaw all of them 7 eggs are expected to survive, 6 eggs are expected to fertilize. If three embryos were transferred her chance for delivering a baby is 20% (the remaining three embryos are frozen). If The first cycle does not succeed and the next three embryos were transferred, her cumulative chance for having a baby from the original egg freezing cycle is approximately 40%.

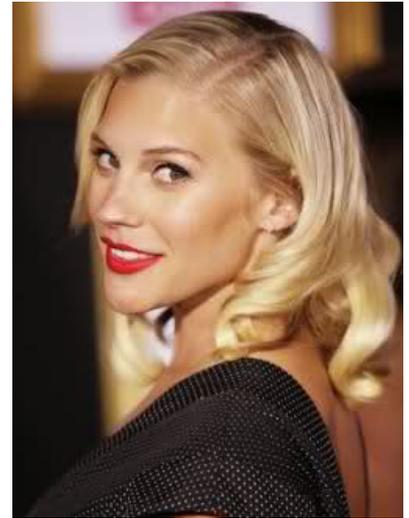
Sorting through statistics of egg freezing is difficult. No single clinic can present convincing statistic due to small number of egg thaw and transfer (not just egg freezing cycles). Most studies present select donors and selected women and not directly applicable to everyone. And then there is the safety issue and lack of long term follow up data related to

safety and health of newborns.

Age is most important predictive of success of egg freezing followed by method of freezing. Vitrification much better than older slow freezing methods. There is now reasonable body of data, though not definitive, that allows prediction of outcome for egg freezing using vitrification based on age and the expected number of retrieved oocytes. It is neither accurate nor scientific to label egg freezing with terms such as [reliable and guarantee](#). It certainly is not a guarantee of children. What is more productive is to i. try to avoid egg freezing through trying to conceive. If not possible, in a short while, then ii. understand your own personal chances of delivering a healthy baby through egg freezing and if they seem reasonable to you consider the procedure, taking in consideration the limitation of available data and filtering out the marketing hype.

[Thyroid Cancer and Future Fertility](#)

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Thyroid cancer is diagnosed in 45,000 individuals each year in the US. Its treatment may affect future fertility in men and women. It is more common in women with female to male ratio of 3 to 1. It is the most rapidly rising cancer in women living in the US. Thyroid cancers are commonly diagnosed in young women in their reproductive years. Treatment of thyroid cancer generally yields excellent results, with the majority of women surviving 10 years or more after diagnosis. Some women develop thyroid cancer due to iodine deficiency in diet or prior neck radiation. Some types of thyroid cancers are related to inheriting an abnormal gene.

Several types of thyroid cancer are recognized 1. Papillary cancer 2. Follicular cancer 3. Medullary cancer 4. Anaplastic cancer 5. Thyroid lymphoma. Papillary and follicular cancers are less invasive tumors and are encountered in the majority of women diagnosed with thyroid cancer. They also respond to estrogen as they carry estrogen receptors. Estrogen may promote growth of thyroid cancer cells. Thyroid cancers are usually suspected on neck examination followed by ultrasound or Iodine scan then biopsy. In general, treatment of thyroid cancer require total thyroidectomy-surgical removal of the thyroid gland followed by radioactive iodine to ablate any thyroid remnants. This is followed by long term thyroid

hormone replacement. Long term follow up is required after treatment.

Effect of thyroid cancer treatment on the ovary

Thyroidectomy followed by thyroid hormone replacement is not known to affect future fertility in men and women. Radioactive iodine can affect the number and quality of eggs remaining in the ovary. The effect is dependent on the dose of radioactive iodine and the age at treatment. Twenty to 30% of women experience transient amenorrhea or irregular menses starting about 3 months after treatment. Normal menses resume about 6 months later. Permanent ovarian failure is rare but may occur in women at age 40 or older at the time of treatment. Increased incidence of miscarriage is reported in the first year after treatment. With the exception of miscarriages, there is no evidence that exposure to radioiodine affects the outcome of subsequent pregnancies and health of borne children.

Effects of radioactive iodine treatment on the testes

Effect of radioactive iodine treatment may be more severe in men. and is related to the total dose of radioactive iodine received. Transient reduction in testosterone and sperm count may occur but sometimes permanent reduction in sperm count and testosterone levels. Men who received large total dose sometimes sustain permanent damage to the testes with absence of ejaculated sperm-azospermia. There is no evidence of effects of radioactive iodine on their newborn children, although its advised that men avoid fathering children for 6 months after treatment.

Options for fertility preservation

Men interested in future fertility should consider sperm freezing prior to radioiodine treatment. Women should also consider fertility preservation if they will be treated with radioactive iodine and are older than 35 years. Radioiodine treatment will reduce their ovarian reserve. In addition they will be required to avoid pregnancy for a year or so. Options available for preservation of fertility in women include ovarian stimulation and egg retrieval followed by egg or embryo freezing. Ovarian stimulation can be modified to avoid estrogen exposure during stimulation. Moreover, in familial thyroid cancers, embryos can be genetically tested to avoid transmission of the abnormal gene to children. Men and women diagnosed with thyroid cancer can benefit from consultation with a fertility preservation specialist prior to treatment to discuss effects on gonads and methods to preserve future fertility. Read more at <http://nycivf.org>

Fertility in Men Diagnosed with Cancer

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Who needs to consider preservation of Fertility?

a. The American Cancer Society estimates that 760,000 men will be diagnosed with cancer in 2009. Cancer itself (before treatment) is sometimes associated with less sperm production in men. This is specially the case in Hodgkin's lymphoma,

testicular cancer, prostate cancer, leukemias and colon cancer. The most harmful factor, however, is cancer treatment. Chemotherapy and radiation significantly impair sperm production. The effect of chemotherapy depends on age, drug used, dose and duration. Cyclophosphamide appears to be the most harmful agent. Radiation also impairs sperm production especially at doses of 1200cGy or more.

Sperm count sometimes recover to a variable extent years after cancer treatment. This depends on the type of cancer and treatment used. For example 90% of men diagnosed with Hodgkin's lymphoma, treated with MOPP chemotherapy regimen, do not have any sperm in the ejaculate after one year.

b. Bone marrow transplantation for cancer of nonmalignant diseases usually require prior irradiation and chemotherapy. This is associated with high risk (85%) of complete failure of sperm production.

c. Connective tissue / autoimmune diseases as lupus and rheumatoid arthritis requiring treatment with chemotherapy.

d. Genetic abnormalities associated with rapid loss of male germ cells e.g. Klinefelter syndrome, Y chromosome microdeletion (AZFc).

Methods used for Fertility Preservation

Methods used to preserve fertility in men are generally divided into two categories:

Protection of the testes from damage caused by cancer treatment:

1. Shielding the testes from radiation field.
2. Protection of the testes from the effect of chemotherapy.

GnRH agonists are a group of medications that suppress the master gland in the brain, preventing the release of the

hormones that stimulate sperm production in the testes. Although suggested, there is no proof that they actually increase the odds for pregnancy after the use of chemotherapy. Actually, there is no effective protective medication available for use in men or women.

Low Temperature Storage of Sperm and Testicular Tissue:

a. Sperm Cryopreservation. This is the standard method for preservation of fertility in men. A sperm sample is obtained by masturbation and frozen for later use. If feasible multiple samples are obtained. In the future, sperm sample are used for intrauterine insemination or IVF / intracytoplasmic sperm injection (ICSI). Banking sperm was found to offer not only a chance to father children in the future but also encouragement and improved morale during disease treatment especially if it was initiated by the patient own initiative.

Lack of information and counseling is the most important reason why men diagnosed with cancer do not bank their sperm.

Although freezing may reduce the quality of sperm especially if it was not optimal before freezing, modern reproductive medicine can handle the majority of compromised specimens yielding excellent pregnancy rates, similar to those of fresh sperm.

b. Testicular Sperm Extraction (TESE). This surgical procedure retrieves sperm from inside the testes if no sperm was found in the ejaculate. If this procedure is used before cancer treatment, sperm are retrieved in over 50% of cases. Sperm or testicular biopsies are frozen for later use. ICSI is used for fertilization. In case of testicular cancer, sperm retrieval can be performed at the same time of surgery for cancer.

c. Testicular Tissue or Germ Cell Freezing. This is an experimental technique. Immature germ cells or testicular pieces are frozen for later transplantation. No pregnancy was achieved using this method so far.

In conclusion, fertility-sparing strategy is readily available to the majority of men at risk for diminished fertility through sperm cryopreservation. Men interested in fathering children in the future should be counseled about this option.