

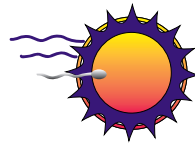
# LA JOLLA IVF

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# LA JOLLA IVF

## REPRODUCTIVE OPTIONS FOR PATIENTS DIAGNOSED WITH CANCER

Over the past twenty years medical science has dramatically increased the survival rates of oncology patients. Combination chemo and radiation therapy regimens are being designed to avoid the acute toxic effects of these treatments, however, many young patients still face post-treatment compromise of their fertility with potential difficulties in the future to have a family.

### A) Preservation of Male Reproductive Options

#### 1) Sperm Freezing:

The simplest option for fertility preservation in males is cryopreservation of sperm prior to initiation of treatment. Historically, both the efficacy and safety of utilizing cryopreserved sperm has been demonstrated. Gonadotoxicity in males is dependent on the stage of spermatogenesis (sperm development). Damage to mature sperm while sparing the stem cells results in temporary diminishment of spermatogenesis. However, damage to the stem cells will result in probable permanent impairment of spermatogenesis. The simplest and most efficient option in males is freezing of the sperm prior to the initiation of treatment for cancer. History has proved both the safety and efficiency of utilizing sperm that was cryopreserved before cancer treatment in helping these men to father children.

#### 2) Sperm Aspiration with IVF and ICSI:

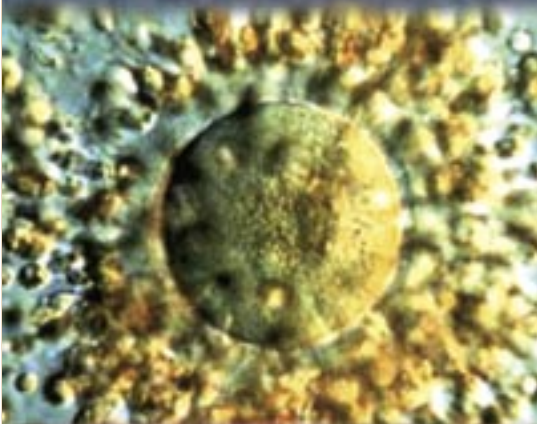
There are now a number of recent advances that have further expanded the reproductive options in men who have already undergone cancer treatment. Some of these men are azospermic by semen analysis, however sperm can be retrieved via epididymal or testicular aspiration in the doctor's office. If this sperm is not damaged from the chemotherapy then it can be used in an IVF cycle with ICSI (the injection of the sperm directly into the oocyte).

### B) Preservation of Female Reproductive Options

Unfortunately, the preservation of fertility in women undergoing cancer treatment is much more complex than in men. In addition, in women many cancers directly affect childbearing functions. For example, radiation can adversely affect the uterus by either reducing its blood flow or affecting the endometrium. Also, both chemo and radiation therapy may impair germ cell function. Women are born with a finite number of oocytes and these diminish as women age. The rate at which primordial follicles regress is accelerated with cytotoxic therapy.

#### 1) GNRH Suppression:

Studies have shown that girls undergoing chemotherapy prior to the onset of puberty have improved ovarian and reproductive function compared to those receiving



chemotherapy post puberty. There is some evidence that suggests that GNRH agonists minimize the toxic effect of chemotherapy on the ovary by inhibiting the process of follicular recruitment and then follicular maturation. As the GNRH agonists take a few weeks to suppress follicular recruitment, this therapy should be started prior to the initiation of chemotherapy. However, this approach may cause an unacceptable delay in treatment.

## 2) Oocyte Freezing:

Until recently cryopreservation of unfertilized eggs has still been considered experimental. We can now offer several approaches to the cryopreservation of oocytes:

a) Patients can attempt to preserve and utilize mature oocytes. The downside of this approach is that the patient has to undergo ovulation induction prior to retrieving their oocytes. Again with this approach there may be a delay in cancer treatment, even though it would probably be only 2 to 3 weeks. The freezing of mature oocytes seems better suited to the preservation of fertility in single females who are looking at the possibility of freezing oocytes while still fairly young as insurance against age-related infertility. With newer freezing techniques some success has been achieved.

b) Alternatively, immature oocytes can be retrieved prior to maturation. This approach allows for the extraction of multiple oocytes without a waiting period for ovulation induction. Dr. Tucker Ph.D, H.C.L.D., who is the Science Director of La Jolla IVF's Embryology Lab was involved with the first pregnancy in the world achieved from immature eggs that were frozen, subsequently thawed and then matured in the IVF Lab. Immature eggs appear to survive the freezing process relatively well and they possess certain features that help maintain their integrity during the stress of cryopreservation. Their membranes are more permeable to the cryoprotectant and their chromosomes are more safely packaged in the nucleus which

protects them from disruption. This technology is still in the early stages of development but potentially holds great promise for patients undergoing chemo and radiation therapy.

c) A few IVF labs are looking at preserving ovarian cortical stripes. This potentially allows for the preservation of thousands of oocytes. Successful ovulation induction with egg retrieval from ovarian tissue transplanted under the forearm has been performed. However, this procedure has the disadvantage of potentially transplanting microscopic tumor cells.

d) The multiple potential routes for cryostorage of the egg may actually be dictated by the different clinical needs of the situation. The choice as to whether to use whole ovarian tissue freezing, separate ovarian follicle storage, or cryopreservation of mature or near mature oocytes will certainly be decided on a case by case basis.

## 3) Embryo Cryopreservation:

Embryo cryopreservation is another alternative that may allow women to complete their cancer treatment with subsequent initiation of childbearing at a future date. In some patients ovulation induction can be used after cancer treatment without the potential for increasing the chances of a recurrence of the cancer. In those patients when ovulation induction is not feasible at our center we encourage these women to accumulate embryos by going through "natural cycles." The patient's egg is harvested after going through a natural cycle which we monitor. The egg is then fertilized and the resulting embryo is frozen. After going through several such natural cycles, enough frozen embryos will have accumulated for either the patient herself or a gestational surrogate to go through a frozen-thaw cycle. This approach can offer realistic pregnancy potential for patients who cannot take fertility medications or carry a pregnancy due to their previous cancer.

## 4) Pelvic Radiation Therapy:

In patients undergoing radiation therapy to the pelvis, if extreme care is used to minimize damage to the ovaries, this approach can really help

diminish the cytotoxic effect of radiation on the ovaries. Patients receiving external beam brachytherapy should have unnecessary ovarian exposure minimized through careful positioning and use of padding. In some patients it may be feasible to surgically transpose the ovaries out of the pelvis. A laparoscopic surgery can fix the ovary to the psoas muscle. This surgery can be done as an outpatient and should not delay radiation therapy. Unfortunately, many times the uterus cannot be spared from the effects of radiation. In these women subsequent childbearing should be with a gestational surrogate.

## Conclusion:

In patients of reproductive age who are undergoing cancer therapy, future fertility should be addressed as a consideration. For men, sperm freezing is the most appropriate and viable option. If the patient can start to store sperm almost immediately after their cancer diagnosis, they can freeze a viable amount of sperm in a short time. This sperm can ultimately be used to generate a pregnancy probably through IVF with ICSI.

In women, embryo cryopreservation and potentially egg freezing can be employed where appropriate. Also GNRH agonist/chemotherapy can be offered to female patients to reduce gonadotoxicity while undergoing chemotherapy.

Patients of reproductive age are usually very interested in hearing about options for preserving their future fertility and are most grateful when their urologists, gynecologists, surgeons and/or oncologists can address this issue in a meaningful way.

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