

Fertility preservation

SOCIAL AND MEDICAL PRESERVATION

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What fertility preservation is...

Fertility preservation is the process of saving or protecting oocytes, sperm, or reproductive tissue so that a person can use them in order to have biological children in the future.

Who can benefits from fertility preservation?

- Those people with certain diseases or disorders, and life events that affect fertility.
 These include people who:
- Have been exposed to toxic chemicals
- Have endometriosis
- Have uterine fibroids
- Are about to be treated for cancer
- Are about to be treated for an autoimmune disease
- Have a genetic disease that affects future fertility
- Delay having children



The decline of the number of children per woman since 1950

In the past people had many more children than today. The number fluctuated over time and there were some differences between countries, but for much of our history, the average woman had at least five children.



Note: Children per woman is measured as the total fertility rate, which is the number of children that would be born to the average woman if she were to live to the end of her child-bearing years and give birth to children at the current age-specific fertility rates.

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Fertility preservation. Why is it important?

- The evolution of **assisted reproductive technologies** (ART) has facilitated the development of methods and strategies to preserve fertility in patients with cancer. (Medical preservation)
- Some of the fertility preservation methods are also used in women with medical indications other than cancer and in women who seek fertility preservation for Social reasons.



Medical fertility preservation

Fertility is a key aspect of quality of life for cancer patients in childbearing age.

Preservation of fertility is defined as the application of medical, surgical and laboratory procedures to preserve the potential of genetic parenthood in those people at risk of sterility.

Decrease or loss of fertility can take place due to exposure to chemotherapy, radiation or surgery.



Cancer effects..

The degree of damage is dependent upon:

- the type of the chemotherapeutic agent used,
- dose given,
- age of the patient,
- baseline of ovarian reserve.
- Reduction in ovarian reserve occurs because of apoptosis of the growing follicles and activation of the resting follicle with subsequent apoptosis, leading to a **burn-out** effect.



From complete amenorrhea to premature menopause

Medical fertility preservation

- The American Cancer Society estimates that cancer affects one in each 3 women living in the United States.
- But recently the number of cancer survivors is increasing worldwide

Quality of life of survivors = Quality of life of healthy people

Estimated and projected number cancer survivors in the United States from 1977-2022 by years since diagnosis



de Moor JS, Mariotto AB, Parry C, Alfano CM, Padgett L, Kent EE, Forsythe L, Scoppa S, Hachey M, and Rowland JH. Cancer Survivors in the United States: Prevalence across the Survivorship Trajectory and Implications for Care. Cancer Epidemiol Biomarkers Prev. 2013 Apr;22(4):561-70. doi: 10.1158/1055-9965.EPI-12-1356. Epub 2013 Mar 27.

LET'S PRESERVE FEMALE FERTILITY

Current Fertility Preservation Techniques



Now we are going to consider all the techniques and methodologies, which aim to preserve reproductive functions when gonadotoxic treatments are applied.

- A pharmacological expedient of ovarian protection during chemotherapy is gonadotrophin- releasing hormone (GnRH) agonist
- It is thought that in the ovary, GnRH agonist decreases vascularity, thereby reducing the concentration of the chemotherapeutic agents.



Despite positive results, the quality of evidence was low in all the studies and for

these reasons its efficiency remains controversial

Ovarian transposition

- Young patients scheduled for pelvic irradiation may undergo oophoropexy to shield their ovaries or move them as far as possible from the radiation field.
- The procedure may complicate future oocyte retrieval and promote some ovarian dysfunction and cyst development.



Stimulating the development of multiple follicles is a prerequisite in ART to maximize the gain of aspirated oocytes. This is crucial in patients with cancer undergoing egg collection for fertility preservation, because they usually have time for only a single attempt before starting chemotherapy.



Cryopreservation is the most diffuse technique used for fertility preservation!

What is Cryopreservation?

- Is that process in which is used a very low temperature to preserve structurally intact living cells and tissue, all biological processes are suspended and material does not decompose.
- Cryobiology principles and the precise control at each step during the process are essential to achieve good results.







• Why LIQUID NITROGEN?

- Chemically inert
- Relatively low cost
- Non toxic
- Non flammable
- Readily avaible



About Cryopreservation

CRYOPROTECTANS

- Higher degree of cell survival during freezing
- Protect cell membrane from freeze-related injury
- High solubility
- Low toxicity at high concentrations
- Low molecular weight
- Ability to interact with water via hydrogen bonding

Cryoprotectants (CPs) are macromolecules added to the freezing medium to protect cells from the detrimental effects of intracellular ice crystal formation.



About Cryopreservation

- Oocytes are unique cells; Their large size, spherical shape and general fragility explain many of the difficulties that occur during cryopreservation.
- Oocytes are particularly sensitive to cooling and are susceptible to cryo-injuries.
- The spherical shape of the oocyte confers a disadvantage; large spherical object, such as an oocyte, has the lowest surface area/volume ratio than any geometric shape.



The main physical stresses associated with cell cryopreservation are cryo-injuries and ice crystal formation.

About Cryopreservation

► VITRIFICATION

- The introduction of oocyte vitrification technology has significantly improved the outcome of oocyte cryopreservation, which lead to pregnancy and live birth rates comparable to those achieved in IVF with the use of fresh oocytes.
- However, there are many concerns about oocyte vitrification:
- Toxic concentrations of cryoprotectans,
- temperature and duration of exposition,
- volumes and characteristics of cryo-containers used.





BABY-MAKING ONICE

Cryopreservation of embryos

- standard method for preservation of fertility.
- Its suitable for women with a male partner or accepting the use of donor sperm.
- This method requird stimulation of the ovary with medications, the eggs are then pick up from the ovary using a procedure under sedation and then fertilized in the laboratory, the resulting embryos are frozen 2 to 6 days later and stored for later use.
- Cancer treatment can start immediately after egg retrieval. After recovery, women can request to use their embryos, that are placed back into the uterus after simple preparation of the lining of the uterus.
- The transfer of two embryos into the uterus yields a pregnancy rate of about 30%.



Cryopreservation of embryos

ADVANTAGES

Well established method

DISADVANTAGES

- Need for a male partner or donor sperm
 - Need for ovarian stimulation (therefore
 - may case a delay in cancer therapy)
 - Only limited number of embryos can be
- obtained
 - Not available in children

Cryopreservation of oocytes

It is considered for women with no male partner and declining the use of donor sperm. It requires stimulation of the ovaries and oocytes retrieval.

ADVANTAGES

- Relatively well established method
- Suitable for those who don't have a male partner
- or don't want to use donor sperm
- Suitable for those who refuse embryo freezing for religious/ethical reasons



DISADVANTAGES

- Need for ovarian stimulation (therefore may case a delay in cancer therapy)
- Only limited number of oocytes can be obtained
- Not available in children

Ovarian tissue cryopreservation

ADVANTAGES

- Does not require ovarian stimulation, therefore can be performed immediately
- Does not require sexual maturity, therefore the only method can be performed in childhood
- Restores global ovarian function (natural conception becomes available)
- Doesn't require male partner/donor sperm

DISADVANTAGES

- Still experimental
- Not clear whether it is safe in
- leukemias



Ovarian tissue cryopreservation – the technique





Autotransplantation

- After complete recovery of the patient
- Orthotopic/heterotopic
- After 4-5 months, endocrinological functions restored
- Lifetime of the transplanted tissues are 4-5 years average



HISTOLOGICAL EXAMINATION OF THE FROZEN TISSUE



In vitro maturation of oocytes

- In this method a very short ovarian stimulation for 3 to 5 days is performed followed by retrieval of immature eggs.
- Eggs are then matured in the lab, fertilized and the resulting embryos are frozen for later use.

The efficiency of this method is lower than retrieving fully mature oocytes. Approximately 70% of the eggs reach maturity in the lab and about 70% of those fertilize with ICSI. This method is suitable for women demonstrating high response to stimulation to fertility medication.



LET'S PRESERVE MALE FERTILITY





Male fertility preservation

- Like women, men are also diagnosed with diseases that directly or not impair future fertility. This is specially important since the intervention to preserve future fertility in men is **easier and less invasive** compared to women. 50–70% of men diagnosed with cancer wanted children in the future.
- Only 24% of young cancer patients banked sperm. The most common reason of bank sperm failing is the lack of informations.



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

1) Protection of the testes from damage caused by cancer treatment



2) Low Temperature Storage of Sperm and Testicular Tissue



PROTECTION

- Shielding the testes from radiation eld.
- 2. Protection of the testes from the effect of chemotherapy.
- GnRH agonists. Although suggested, there is no proof that they actually increase the odds for pregnancy after the use of chemotherapy.



GnRH agonists

Initial overstimulation of GnRH receptors leads to an increase in LH and testosterone production.

Chronic administration evenutally leads to suppression of LH, resulting in suppression of testosterone.



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. In the future sperm sample are used for intrauterine insemination or IVF or ICSI. Banking sperm was found to offer not only a chance to father children in the future but also improved psychologically during disease.



Testicular Sperm Extraction

This surgical procedure retrieves sperm from inside the testes if no sperm was found in the ejaculate. Sperm or testicular biopsies are frozen for later use and ICSI is used for fertilization. In case of testicular cancer, sperm retrieval can be performed at the same time of surgery for cancer.



TESE PESA MESA

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.





Social Fertility preservation

- We define social fertility preservation as an attempt to increase the likelihood of conception, where healthy females and males collect and then freeze their gametes for own use at a later stage in life.
- FP techniques have been used to enable women to postpone pregnancy to a later date for social reasons such as employment or studying.
- For men is relatively easier and have a less impact on life



Social Fertility preservation

- A new question arising with this development is what to do with left-over oocytes. As with embryos, the possibilities are:
- donation for reproduction,
- donation for scientific research,
- destruction.
- Donation of a limited number of oocytes may also take place in the context of a 'freeze and share' arrangement as developed by a British fertility centre (Atalla, 2008).



Fertility preservation options in transgender people

Gender affirming procedures adversely affect the reproductive potential of transgender people. Thus, fertility preservation options should be discussed with all transpeople before medical and surgical transition.

Gender affirming hormone therapy for **transgender women** usually involve:

- androgen lowering medications,
- estrogens.

♀ – ♂

There are multiple forms of testosterone for inducing virilization in **transmen** including parenteral formulations and transdermal preparations. Testosterone acts directly on end organs and **induces male secondary sex characteristics**.

Fertility preservation options in transgender people

Available options for fertility preservation in transgender women

- Semen cryopreservation obtained from masturbation is a standard FP protocol.
- Another option is surgical sperm retrieval (SSR), a surgical procedure that retrieves sperm directly from parts of the testis or epididymis.
- there is no available means of preserving fertility in transgender girls who have not yet undergone spermarche. Testicular tissue and spermatogonium stem cell (SSC) cryopreservation may become viable options in the future.



Fertility preservation options in transgender people

Available options for fertility preservation in transgender men

- Available FP procedures in transmen are embryo cryopreservation, oocyte cryopreservation, and ovarian tissue cryopreservation.
- In prepubertal transboys, the only available option is OTC, but is still considered as an experimental procedure and is not widely available.

Transgender men using hormone therapy may find the oocyte cryopreservation process difficult due to the need to temporarily stop taking the virilization hormone for quite time. Cessation of testosterone could lead to unwanted physical changes and resumption of bleeding which may aggravate feelings of gender dysphoria. In addition, gynecologic procedures such as pelvic examination, transvaginal ultrasound and transvaginal oocyte retrieval could also cause emotional instability and psychological distress for some transmen.

Future methods

Artificial gametes

- The creation of artificial gametes from somatic cells is a theoretical fertility treatment that would benefit anybody. This includes infertile patients with azoospermia or premature ovarian failure, or transgender people who have already undergone gender affirmation surgery.
- Primordial germ cells, pluripotent stem cells and induced pluripotent stem cells are theoretical sources of gamete production.



- In 2016, Zhou et al
- in November 2016, Hikabe and colleagues

Conclusions

Refrost your mind, froze your gametes !

....don't forget to promote fertility preservation !

