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## CRYOPRESERVATION OF GAMETES AND POSTHUMOUS REPRODUCTION –ISSUES AND CHALLENGES

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### ABSTRACT

*Advancement in assisted reproductive technologies made it possible to cryopreserve egg cells and sperms to achieve conception by using cryopreserved gamete. Cryopreservation of human gametes is of great significance in assisted reproductive technologies and has been helping infertile couples to have genetically related children. One of the latest applications of cryopreservation has made possible Posthumous assisted reproduction. Posthumous conception can take place after the death of the genetic father, the genetic mother, or both genetic parents.*

*Posthumous Assisted reproduction can be done using frozen egg, sperm, and embryo. Sperm can also be retrieved from corpse a procedure called Post-mortem sperm retrieval (PMSR) and conception is successfully achieved. However this has also introduced countless ethical, legal, and social challenges. Draft ART bill 2015 has no clear guidelines on procedure for Post-mortem sperm retrieval (PMSR). A better understanding of ethical legal and medical issues involved in ART is essential to protect the welfare and rights of children born through these modern technologies.*

**Key words:** Cryopreservation, gametes, posthumous assisted reproduction, cryo-protectants.

## **Introduction**

Cryopreservation of a cell involves the cooling of a cell and storage at a temperature where all metabolic processes are arrested. In practice, frozen cells are stored at the temperature of  $-196^{\circ}\text{C}$  in liquid nitrogen. Cryopreservation is a way of preserving germplasm that have applications in agriculture, aquaculture, biotechnology and conservation of threatened species (1, 2). The cryopreservation of reproductive cells is the process of freezing, storage, and thawing of gametes. It involves an initial exposure to cryoprotectants cooling to subzero temperature, storage, thawing, and finally, dilution and removal of the cryoprotectants, when used, with a return to a physiological environment that will allow subsequent development. Cryopreserved cells and tissues can endure storage for centuries with almost no change in functionality or genetic information, making this storage a highly attractive method (3). Cryopreservation of human gametes embryos and fertility related tissues are of great significance in assisted reproductive technology (4). In general, ART procedures involve surgically removing eggs from a woman's ovaries, fusing them with sperm in the laboratory, and transferring embryo into woman's uterus or donating them to another woman.

## **Cryopreservation of gametes**

Cryopreservation of human sperm has been developed for assisted reproductive programs for many different reasons, including development of assisted reproductive technologies such as intra-cytoplasmic sperm injection, "fertility insurance" for potential illness-induced infertility early in childhood, and for azoospermic patients (5). In pre pubertal boys undergoing gonadotoxic therapies, cryopreservation of immature testicular tissue is an option to preserve fertility, in the hope that future technologies will allow its safe utilization (6). The intracytoplasmic sperm injection (ICSI) procedure has ability to achieve high fertilization and pregnancy rates regardless of semen characteristics. Palermo et al., in 1992 reported the first birth of baby from intracytoplasmic sperm injection (ICSI). It marked a new era in the treatment of azoospermic patients (7). Cryopreservation of human spermatozoa has overcome many time and space limitations since its introduction in the 1960's and now forms an integral part of assisted reproductive technologies (8). It is increasingly common for men especially soldiers, and athletes to store sperm for potential use by a wife or a partner in the event of their deaths. Cancer patients before proceeding for Chemotherapy also deposit in the sperm bank. Most of these men

hope to use the sperm themselves in the future (9). In the United States, while pre-deployment fertility preservation by soldiers is privately organized and funded, it is reported as a growing and accepted trend among soldiers deployed to Iraq, Afghanistan, and the Middle East. Some even want to bank the sperm before the smallpox and anthrax vaccinations (10). A number of British soldiers posted in war-torn Afghanistan are said to be freezing their sperm in case they are killed or maimed (11). Mammalian embryos have been successfully frozen and stored since 1972, when Whittingham et al., obtained live mice after the transfer of frozen-thawed morulae (12). Since then embryocryopreservation has become routine procedures in human assisted reproduction. In 2010, the Jones Institute for Reproductive Medicine at Eastern Virginia Medical School (Jones Institute) reported yet another milestone in reproductive medicine: the birth of a healthy baby boy from a 20 year old frozen embryo (13). However, embryo cryopreservation raises ethical and legal issues especially in the event of death or separation of couples, wherein deciding the ownership of embryos becomes very difficult. Chen in 1986 reported the first human pregnancy with cryopreserved oocyte. After 10 years in 1997, Porcu et al. reported the first live birth of a healthy baby from cryopreserved oocyte (14). Since then Oocyte cryopreservation is being introduced into clinical practice and is considered to be more acceptable. Oocyte cryopreservation is one of the few options available to keep the fertility potential of patients undergoing chemotherapy and radiotherapy (15). Oocyte cryopreservation or freezing of a woman's eggs is stated to be an option to extend fertility and delay motherhood. Silicon Valley technology giants have offered \$20,000 to both full-time and part-time women employees to freeze their eggs and \$480 annually to store them in order to enable these women to focus on their careers and delay child bearing (16). Cryopreserving of eggs has become a standardized procedure and such cases are reported in India where the child was born out of an egg that was frozen eight years ago (17). All these may possess big challenges and leads to ethical and legal issues, as many gamete cell banks are booming up in our country with very little of them following regulatory guidelines. Our legal system has not even begun to touch some of these technologies.

### **Posthumous Reproduction and challenges**

Cryopreservation of gametes and embryos also allows for children to be conceived after the death of their genetic parents through the process of posthumous assisted reproduction (PAR).

Posthumous reproduction is the birth of a child after the death of a parent. Posthumous births have always occurred, in cases where a husband died from illness, accident, or war before his pregnant wife could deliver their child. This term was developed hundreds of years ago to recognize the paternity of children born to sailors while at sea (18). Advances in reproductive technologies have given birth to a whole new aspect of posthumous reproduction—conception after death of a parent. Rothman first reported viable post-mortem retrieval of sperm in 1980 from a 30-year-old man who became brain dead after a car accident (19). The first pregnancy after post-mortem retrieval of sperm was reported in 1998 and the subsequent birth was reported in March 1999 (20). The Cornell guideline (a set of guidelines addressing post-mortem sperm retrieval) emphasize retrieval must take place within 24 hours of death, cryopreservation must be available locally (21). Although no case has been reported in India, recently the widow of a young man based in Delhi asked the doctors at the All India Institute of Medical Sciences (AIIMS) to retrieve his sperm so that she can have a baby. The parents of the man have also supported the request of their daughter-in-law (22). Since there was no guideline in place for the procedure for PMSR, the request was declined (23). More such requests are bound to arise in the future. It is undoubtedly a breakthrough in medical field, but it raises issues in the event of death of the man, child's right on man's property, and more importantly psychological impact on children. More importantly the consent of the deceased is essential in post-mortem sperm retrieval.

Although draft ART bill 2015 is ready, there are no clear guidelines on procedure for postmortem sperm retrieval (PMSR) in our country (23). The guideline must include the duty and responsibility of hospitals and physicians in dealing with such issue. The guideline should address, whether in the absence of the consent from the deceased for PMSR, can the widow of the deceased request for sperm retrieval? Whether the parents of the deceased can claim? Embryo cryopreservation has been prompted by the surplus embryos generated during IVF and embryo transfer programs. The ability to store embryo for a longer period of time brings up all sort of legal and ethical issues. In certain instances, donors may not be able to keep in contact with the fertility clinic and over the period of time and fertility clinic also fail to locate the donors. In such situation it difficult to determine the fate of embryos. Can it be donated? If so, who decides? Does the child has any right to know his/her biological parents? What if child born from donated embryo develops serious genetic disorders? These are some of the perceived issues which law has to answer. A nationwide survey conducted by the American Society of

Reproductive Medicine and the Rand Corporation found that 400,000 unused frozen embryos are currently being stored in fertility clinics (24). Cryopreservation of sperms/oocytes raises the possibility that gamete cell banks may 'sell' the sperms/oocytes to other men/women or researchers who are in the market for egg/sperm donors. A Houston man has launched a unique court battle, claiming his twin sons resulted from his sperm being stolen and taken to a Houston fertility clinic without his knowledge (25). Ability of cryopreserved embryo to survive its biological progenitors and subsequent posthumous conception raises issues on inheritance law and social security benefits. In USA, Supreme Court hears a rare and complex case on whether twins conceived artificially after their father's death count as his children(26). One of main legal issues arising from posthumous conception is parentage. Can the deceased gamete providers be considered as parents of posthumously conceived children? Is the child entitled to citizen ship rights and social security benefits? Very few countries have well defined legal system to address these issues (27). Gametes belong to the individual and it is the individual to decide the fate of his/her cell. While several countries talk about the rights of deceased donors, very few in fact none speaks about the rights of children born through these technology.

With advancement in medical field it is possible to extend the motherhood and pregnancies.

Even in India there are reports of deliveries beyond the age of 70 years. But one must also think about the well-being and rights of children. Who is responsible for any kind of injury incurred to the gamete cell during storage, (which may go unnoticed) which later find way to uterus and subsequent birth? New reproductive technologies have been introduced so rapidly that ethics and the law have been unable to respond appropriately. Can the law respond to potential wrongful birth and wrongful life suits resulting from sperm/embryo switching and wrongful conception? Banking of human sperm/oocytes has to be performed in a safe and controlled way. Cryo banks should do a quality check of gametes and screen gametes for serious genetic and infectious diseases before considering for freezing. There are reports of how world courts are facing challenges when dealing with cases of wrongful life.

## **Conclusion**

Modern biotechnologies are assisting and changing the concepts of reproduction. India too is adopting these assisted reproductive technologies. Posthumous conception opens the door for significantly more complex familial relationships. At times court is unable to tackle the issues

emerging from modern reproductive techniques, be it surrogacy or, becoming father through surrogacy.

India has an estimated number of around 800 plus fertility clinics across the country and new clinics are being added every day. India is also a favorite destination for surrogacy. However the biggest challenge is lack of regulatory frame work. Functioning of gamete cell banks and gamete donation need to be strictly regulated. Though India so far have not reported any case of posthumous assisted reproduction, problem can arise in future. Hence it is essential to have regulations in place to protect the rights of children born through these technologies.

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