NIMAAYA

OOCYTE VITRIFICATION

TOPICS

- How does Assisted Hatching work?
- Who should be treated with Assisted Hatching
- Your treatment options explained

About this booklet

This series of booklets has been developed and written with the support of leading fertility clinics across Australia, and AccessAustralia — a national organization that provides numerous services for people having difficulty conceiving. We also acknowledge the many people who spoke openly about their own experiences with assisted conception in order to help others experiencing a similar journey. Merck Serono thanks the many individuals, couples and Australian Healthcare Professionals, including fertility specialists, specialist nurses and psychologists who shared their knowledge and expertise during the production of these booklets.

Important notice: The information provided in this booklet does not replace any of the information or advice provided by a medical practitioner and other members of your healthcare team. Your doctor will determine the best medications and course of action for you based on your requirements and conditions.

Prescription medicines have benefits and risks. Use all medications strictly as directed by your doctor and raise any questions or concerns with them before, during or after using prescribed medicines. If you experience side effects consult your doctor.

Full information regarding the medicines listed in this booklet, including how they are taken and side effects, is available from the Consumer Medicine Information (CMI) sheets. These can be found at the TGA website (www.tga.gov.au) for Australian residents and the medsafe website (www.medsafe.govt.nz) for New Zealand residents.

Medication availability and funding criteria may differ between Australia and New Zealand.

Contents

Oocyte Vitrification

Eggs (oocytes) are frozen using either a controlled-rate, slow-cooling method or a newer flash-freezing process known as vitrification. Vitrification is much faster but requires higher concentrations of cryoprotectants to be added. The result of vitrification is a solid glass-like cell, free of ice crystals.

The techniques of Vitrification of Oocytes and the subsequent warming process being used today are now producing results far superior to the results that are obtained with slow-freezing techniques, and it would seem that this is the method of female fertility preservation that will be widely used in the near future. The reported success of the use of this method should stimulate a renewed debate on oocyte storage for fertility preservation without a medical indication. (Fertil Steril® 2008. ©2008 by American Society for Reproductive Medicine.)

While men are capable of manufacturing 1000 sperm in the space of one heartbeat up to a ripe old age, the female of the species steadily but surely loses her eggs from birth to menopause, with an accelerated loss from the mid thirties onward. Accompanying this loss of eggs is an equally severe decline in egg quality with age. Consequently, female fertility potential rapidly dwindles from the age of 37 on.

Sperm cryopreservation was first successfully performed (in snow!) more than 200 years ago. The cryopreservation of oocytes for fertility preservation has been attempted much more recently but has undergone a complex history, which has been largely unsuccessful. The slow-rate freezing of oocytes results in extracellular and intracellular crystallization of ice, which can cause irreparable damage to the spindle. In addition, the egg is particularly sensitive to chilling injury, which assuredly can occur with most slow-freezing protocols.

It now seems that the rapid-freezing method to induce vitrification of oocytes has broken the ice. The first attempts of vitrification of sperm were started about 70 years ago (1, 2). The techniques of vitrification of oocytes and the subsequent warming process being used today are producing results equal to those using fresh oocytes and are, certainly, far superior to those using slow-freezing techniques. In the last 2 years, highly successful survival rates of oocytes of over 90% after vitrification and warming, fertilization rates of 75%–90%, pregnancy rates of 32%–65% per ET, and live-birth rates of over 50% have been reported. Successful deliveries after oocyte vitrification have been reported from countries as far flung as Japan, the United States, Colombia, and Italy and Germany in Europe (3–14). Particularly relevant is a prospective randomized study from Cobo et al. Comparing the outcome of oocyte vitrification (Cryotop method) with that of fresh donor oocytes coming from the same cycle. No significant differences in the excellent clinical outcomes were seen. Similar encouraging results were very recently reported by Nagy et al. In a prospective study, which validate the use of oocyte vitrification for egg donation.

In addition, the vitrification process is considerably less complicated than slow freezing, avoids the complication of intracellular ice crystallization, and is less expensive and time-consuming. The initial worry that the use of the high concentrations of cryoprotectants needed would cause toxic and osmotic effects have so far proved unfounded as long as the eggs are only left in the highest concentration of cryoprotectant for less than 60 seconds.

Assuming that the safety of the vitrification of oocytes will continue to be verified, it would seem that this is the method of female fertility preservation that will be widely used in the near future. The reported success of the use of this method should stimulate a renewed debate on oocyte storage for fertility preservation without a medical indication (assuming that impending ovarian failure is not a medical indication).

The European Society for Human Reproduction and Embryology Task Force on Ethics and Law published ethical considerations for the cryopreservation of gametes and reproductivetissues for self-use in 2004 (17). In clause 2.2, it stated, “In view of the lack of success and clinical application in the case of ovarian tissue, this application (reproductive tissue cryopreservation) should not be offered to women as a means to preserve their fertility potential when there is no immediate threat to their fertility.” In addition, “According to similar reasoning, oocyte freezing for fertility preservation without a medical indication should not be encouraged.” In a similar vein, the Practice Committee of the American Society for Reproductive Medicine released a statement in late 2007 that “oocyte cryopreservation should not be a means for women to delay reproduction”

Should the initial encouraging results continue to flow, we believe that these statements should be reconsidered or, to quote Bob Dylan (circa 1964), "the times they are a changin."

We believe that the time has come to consider redressing the balance between the male and female fertility potential now that we apparently have the technology to do so. While sperm may be naturally capable of inducing a pregnancy even up to the age of 80, the limited reproductive life span of oocytes has restricted women to conceiving and delivering a baby up to the age of 45 at the best but with increasing difficulties from the mid to late thirties onward. The successful preservation of oocytes by vitrification will provide the "aging" woman who has had to delay her childbirth, for any reason, the opportunity to conceive and deliver using her own oocytes at the time she decides.

Society dictates the widespread use of medical advances, and society is seemingly presently intent on women delivering at later ages. The laws of the country will dictate the age limit up to which ET may be performed after the fertilization of previously vitrified oocytes in the same way that the age limit after ovum donation is applied. While ovum donation has been highly successful in providing a solution for women with incompetent oocytes, the preference of using their own genetic material is overwhelming. Legal, ethical, and logistic problems of ovum donation may also be overcome with the use of the subject's own vitrified oocytes.

Some additional considerations with Oocyte Cryopreservation

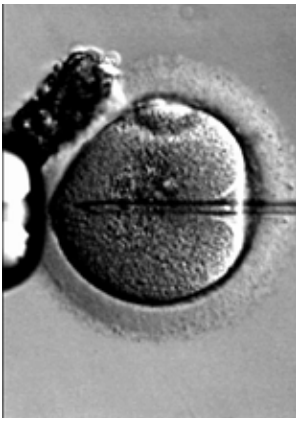
- CSI must be done for fertilization, regardless of sperm parameters. This is due to the hardening of the Zona Pellucida.
- Patients without a partner can opt to freeze some Oocytes, and some embryos (using donor sperm for fertilization).
- ASRM has guidelines about the essential elements of informed consent of elective oocyte cryopreservation. One can argue that a similar outline for counseling be provided to cancer patients who are contemplating oocyte cryopreservation.

- In the absence of clinic-specific outcomes data about live-birth rates after oocyte cryopreservation, ASRM recommends using these estimates based on published literature:
  - 2% live-birth rate per oocyte thawed following slow-freeze methods.
  - 4% live-birth rate per oocyte thawed following vitrification

- The likelihood of success may be significantly lower in women over the age of 35, as most published reports are for younger women.

Oocyte Cryopreservation (Vitrification)

— Oocyte Bank



Oocyte cryopreservation or vitrification (egg freezing) is a rapidly advancing, breakthrough technology in which a woman's eggs (Oocytes) are extracted, frozen and stored (oocyte bank). Later, when she is ready to become pregnant, the eggs can be thawed, fertilized, and transferred to the uterus as embryos.

Unfortunately over 50,000 reproductive-age women are diagnosed with cancer each year in the United States only. Chemotherapy and radiotherapy are toxic for Oocytes, leaving few, if any, viable eggs. Egg freezing offers women with cancer the chance to preserve their eggs so that they can have children in the future.

Oocyte cryopreservation is aimed at three particular groups of women: those diagnosed with cancer who have not yet begun chemotherapy or radiotherapy; those undergoing treatment with assisted reproductive technologies who do not consider embryo freezing an option and those who would like to preserve their future ability to have children, either because they do not yet have a partner, or for other personal or medical reasons.

Oocyte cryopreservation is an important option for individuals undergoing IVF who object, either for religious or ethical reasons, to the practice of freezing embryos. Having the option to fertilize only as many eggs as will be utilized in the IVF process and then freeze any remaining unfertilized eggs can be a positive solution. In this way, there are no excess embryos created, and there is no need of unused frozen embryos disposition, a practice which can create complex choices for certain individuals.

Egg freezing can also be beneficial for women who, for the purpose of education, career or other reasons, desire to postpone childbearing. Freezing eggs at an early age may ensure a chance for a future pregnancy.

Additionally, women with a family history of early menopause have an interest in fertility preservation. With egg freezing, they will have a frozen store of eggs, in the likelihood that their eggs are depleted at an early age.

Method

The egg-retrieval process for Oocyte cryopreservation is the same as that for in vitro fertilization. This includes 2–4 weeks of hormone injections and hormonal contraception in order to stop ovulation, followed by more hormone injections to stimulate ovaries and ripen multiple eggs. When the eggs have matured, additional hormone is given and the eggs are removed with an ultrasound-guided needle through the vagina. The procedure is conducted under sedation. The eggs are immediately frozen (vitrified).

The egg is the largest cell in the human body and contains a great amount of water. When the egg is frozen, the ice crystals that are formed can destroy the integrity of the cell. To prevent this, the egg must be dehydrated prior to freezing. The water is then replaced by a special cryoprotectant to inhibit the formation of ice crystals.

Eggs are frozen using either a Controlled-Rate and Slow Freezing in Cryopreservation or a new flash-freezing process known as vitrification. The slow-freeze method is by far the most practiced of the embryo freezing techniques. Vitrification is a new rapid freezing process in which a high concentration of cryoprotectant is used. The result is a solid glass-like cell, free of ice crystals. This is the method mostly used in CFC.

Additionally, once frozen, the zona pellucida, or shell, of the egg hardens, requiring embryologists to inject the sperm into the egg with a needle in order for fertilization to occur. This technique is called ICSI (Intracytoplasmic Sperm Injection) and is also used in IVF.

Looking for more information?

other booklets in the Pathways to Parenthood series are available at: www.nimaaya.com

- Endometriosis
- Overcoming male Infertility
- Female infertility & assisted reproductive technology (Art)
- Your step by step guide to treating Infertility
- Polycystic ovary syndrome (PCOS)
- Ovulation Induction (OI)
- Intra Uterine Insemination (IUI)
- In Vitro fertilisation (IVF) & Intra-cytoplasmic sperm injection (iCsi)
- Managing the stress of Infertility
- Azoospermia
- Intrauterine Insemination
- Male Infertility
- Laser Assisted Hatching
- Semen Analysis
- Why Investigate for Infertility

NIMAAYA

How can you choose the right IVF centre?

Choosing the right fertility clinic is crucial to make sure that your dream of parenthood is on the right path. While every failed IVF cycle can be a major psychological and financial setback, the abundance of fertility clinics leads to confusion and frustration.

But do not lose hope. There are a few easy checks that any couple can do to help them find the fertility clinic that is right for them.

Facilities

Nimaaya has a full time Embryologist with a Masters in Clinical Embryology, armed with 10 years of intensive experience.

We believe in delivering the best and the latest technology at no added cost to our patients, who have the right to the best medical care, even if they don't live in the metros.

Services

Our centres provide treatment for all types of cases. Our Endoscopy department is capable of Endoscopic treatment of cases like Fibroids, endometriosis and Poly Cystic Ovaries.

Dr. Kishore Nadkarni is our Male Infertility specialist, with 30 years of experience in the field. We provide TESA, PESA and TESE for cases of Azoospermia (NIL SPERM).

Our centre is one of the most cost-effective centres in India with unparalleled success rates.

3rd Floor, Jash Bryant, Opp. Old RTO, Ring Road, Surat–395 001, Gujarat, India.
t. 0261 611 9900 | e. hello@nimaaya.com | w. www.nimaaya.com
Initiative by 21st Century Group of Hospitals