Oocyte cryopreservation – relevance for all medical practitioners in South Africa

To the Editor: This literature review was undertaken to investigate the efficacy of the two different freezing methods currently used in oocyte cryopreservation.

Published literature in which the outcomes of fresh and frozen cycles – both slow- and fast-freeze (vitrification) methods – in assisted reproductive techniques (ART) were reported during the period 1999 - 2009 was reviewed. Metalib was used to search across multiple databases for the period 1999 - 2009, to identify studies that answered the question 'What are the fertilisation, implantation and pregnancy rates achieved when using fresh or frozen oocytes?' The scientific background, current developments and results of these three methods were reviewed. In addition, references of the retrieved articles were hand-searched.

Oocyte cryopreservation has proved to be a useful technique, as it gives women who are about to undergo chemotherapy, radiotherapy or oophorectomy a chance to preserve their fertility. Healthy women can also make use of this technology to preserve their fertility and delay childbearing age. Other non-oncological conditions for desiring fertility preservation may be auto-immune or haematological diseases requiring chemotherapy, and excision of an ovarian cyst, possibly resulting in damage to the ovarian cortex and premature ovarian failure.[1] As a result of this technology, couples who make use of ART may now freeze their oocytes rather than their embryos. Once their family has been completed, it is emotionally much easier to dispose of frozen oocytes rather than embryos.

Cryopreservation of oocytes allows patients to avoid a few of the many ethical, moral and religious issues connected with embryo cryopreservation. However, in contrast to the embryo, the oocyte is more sensitive to the cryopreservation process owing to its high water content, which predisposes it to damage caused by ice crystal formation.

Currently there are two methods for cryopreservation: slow freeze, rapid thaw and fast freeze or vitrification. The slow-freeze method is a time-consuming process, taking up to 3 hours, and requires expensive computerised equipment. Vitrification, or fast freeze, is a far more time-efficient method that does not require costly equipment and is therefore far more economical.

The results of this review compared the outcomes of slow freezing and vitrification methods with those achieved in fresh cycles in ART. Fresh cycles showed fertilisation rates after intra-cytoplasmic sperm injection (ICSI) of between 73.4% and 96.6%, and cleavage rates between 71.5% and 97.9%. Implantation rates per embryo transferred were 5.5 - 39.8% and pregnancy rates per embryo transfer cycle 10.3 - 48.9%. Slow-freeze cycles showed survival rates after thawing of 37.0 - 95.8%, fertilisation rates after ICSI of 45.4 - 89.7%, cleavage rates of 76.5 - 100%, implantation rates per embryo transferred of 2.2 - 62.5%, and pregnancy rate per embryo transfer cycle of 4.2 - 37.5%. Vitrification cycles showed survival rates after thawing of 68.6 - 99.4%, fertilisation rates after ICSI of 70.6 - 93.0%, cleavage rates of 89.8 - 100%, implantation rates per embryo transferred of 6.4 - 45.3%, and pregnancy rates per embryo transfer cycle of 17.6 - 80.0% (Table I).

All three ART methods reviewed here (fresh cycle, slow freeze and vitrification) have varying success rates, which have all shown improvement over the years. Ultimately it seems that with further innovation, vitrification will become the leading method of oocyte cryopreservation simply owing to its time efficiency, the simplicity and safety of the method, and the reduction in costs by eliminating the need for costly machinery. Although initial survival, fertilisation and cleavage rates for cryopreserved oocytes were relatively poor, the advancements made in cryoprotectants and method protocols in the recent past have caused these rates to improve steadily. Oocyte cryopreservation can therefore be offered as a standard

Table I. Comparison of the outcomes of all three methods

Summary	Fresh (9 articles)	Slow freeze (16 articles)	Vitrification (9 articles)
Survival rate		37.0 - 95.8%	68.6 - 99.4%
Fertilisation rate	73.4 - 96.6%	45.4 - 89.7%	70.6 - 93.0%
Cleavage rate	71.5 - 97.9%	76.5 - 100%	89.8 - 100%
Implantation rate/ET	5.5 - 39.8%	2.2 - 62.5%	6.4 - 45.3%
Pregnancy rate/ETC	10.3 - 48.9%	4.2 - 37.5%	17.7 - 80.0% (average 42.8%)

ET = embryo transfer; ETC = embryo transfer cycle.

of care, not only to patients wishing to delay fertility because of imminent cancer therapy but also to couples who refuse embryo cryopreservation or in countries where there are limits on fresh oocyte fertilisation and where embryo freezing is prohibited.

It is important for medical practitioners to take note of the indications for oocyte cryopreservation, which may be both oncological and non-oncological. They are as follows:

Oncological conditions[2]

- **Cancers.** Patients may require ionising radiation or an alkylating agent, which may be gonadotoxic, causing premature ovarian failure and infertility.

- **Cytotoxic agents.** Bone marrow transplants may be used for the treatment of haematological disorders such as sickle cell anaemia, as well as cancerous haematological disease. High-dose chemotherapy is used to destroy existing bone marrow. Auto-immune diseases such as systemic lupus erythematosus, multiple sclerosis and rheumatoid arthritis often affect women of reproductive age, and these diseases are also treated with cytotoxic drugs such as cyclophosphamide or methotrexate.

Non-oncological conditions[1]

- **Surgical menopause** may result from prophylactic oophorectomies (BRCA1 and BRCA2 gene carriers), or repeated ovarian surgery for benign disease such as ovarian cysts or endometriosis, resulting in damage to germ cells.

- **Postponement of fertility** may be due to education, careers or decisions to delay marriage.

The ability to freeze and store oocytes creates a number of opportunities for reproductive medicine. It allows patients to postpone maternity for a number of indications, as well as circumventing the emotional, religious and ethical issues associated with embryo freezing.

Currently approximately 20 - 40 oocytes are necessary to achieve one pregnancy, whereas 100 - 150 were necessary in the past.[3] This indicates that progress has been made with regard to the success of cryopreservation of oocytes, and each method will have its place in reproductive medicine.

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