DOI: 10.1111/tog.12191
The Obstetrician & Gynaecologist
http://onlinetog.org
2015;17:116–124

Review

Female fertility preservation: a fertile future?

Christina M Radon MB ChB BMedSci MRCOG,[a,*] **Amol A Borkar** MBBS MRCOG,[b] **Roy R Homburg** MBBS FRCOG[c]

[a]Registrar in Obstetrics & Gynaecology, Manly & Mona Vale Hospitals, Northern Sydney Health Service District, NSW, Australia
[b]Clinical Fellow in Assisted Conception, Homerton Fertility Centre, Homerton University Hospital NHS Foundation Trust, Homerton Row, London E9 6SR, UK
[c]Head of Research, Homerton Fertility Centre, Homerton University Hospital NHS Foundation Trust, Homerton Row, London E9 6SR, UK
Correspondence: Christina Radon. Email: radonchrista@live.com.au

Accepted on 28 January 2015

Key content
- Fertility preservation is a rapidly evolving branch of reproductive medicine.
- Ovarian senescence, whether physiological or pathologically accelerated, limits the reproductive capacity of women.
- Given the increasing numbers of young women surviving cancer, along with increasing numbers of women deferring childbearing for social reasons, the possibility of fertility preservation is assuming ever increasing importance.

Learning objectives
- To be aware of all fertility preservation options available to young women.
- To acknowledge the appropriate indications or contraindications of individual fertility preservation techniques.
- To gain understanding of the key components central to counselling women requesting advice on fertility preservation.

Ethical issues
- Encouraging cancer patients to undergo fertility preservation treatments could have the potential to negatively impact their disease prognosis.
- Whether fertility preservation is an appropriate allocation of health resources, given that a proportion of women undergoing preservation procedures may remain fertile, may ultimately choose not to pursue parenthood, or, in the case of malignancy, may not even survive their diagnosis.
- The availability of fertility preservation for social reasons could encourage women to delay childbearing, creating a society of 'older mothers' reproducing beyond their natural reproductive lifespan, and thereby potentially creating a new medical burden on society.

Keywords: embryo cryopreservation / fertility preservation / oocyte cryopreservation / oocyte vitrification / ovarian transposition / trachelectomy

Please cite this paper as: Radon CM, Borkar AA, Homburg RR. Female fertility preservation: a fertile future? *The Obstetrician & Gynaecologist* 2015;17:116–124

Introduction

Fertility preservation is receiving increasing attention as an evolving area of reproductive medicine. It aims to preserve reproductive tissue for future use. The main beneficiaries are those requiring gonadotoxic medical treatment, women undergoing destructive reproductive tract surgery, those with genetic conditions associated with premature ovarian failure, as well as women wishing to defer childbearing for 'social' reasons. Box 1 shows the indications for fertility preservation.

Preservation of reproductive tissue is achieved through cryopreservation. Cryopreservation refers to the cooling of cells and tissues to sub-zero temperatures in order to achieve complete cessation of biological activity. The temperature that is generally used for the storage of mammalian cells is –196°C, the temperature of liquid nitrogen.[1] Traditionally cryopreservation was achieved through slow freezing, although attention is now turning to vitrification. Vitrification deploys ultra-rapid cooling, in the presence of high concentrations of cryoprecipitants, to solidify the cell or tissue into a glass-like state. This process avoids ice crystal formation and associated chilling injury, and is of particular importance to the cryopreservation of oocytes, whose large water content is more predisposed to ice crystal formation and damage to the fragile meiotic spindle.[2]

Fertility preservation and malignant disease

Advances in cancer therapy have increased the number of women surviving a diagnosis of malignancy. Unfortunately, many such treatments are gonadotoxic and, as such, public and professional attention to fertility preservation for these women is growing.

Germ cells are inherently sensitive to the toxic effects of both chemotherapy and radiotherapy. In particular, chemotherapy protocols containing alkylating agents, especially cumulative dose regimens of procarbazine and cyclophosphamide, appear to be the most gonadotoxic.

Box 1. Indications for fertility preservation

Gonadotoxic treatment of malignancy	i) Chemotherapy/radiotherapy ii) Reproductive tract surgery
Genetic conditions	i) Turner syndrome ii) Fragile X permutation iii) X chromosome aberrations
Surgery for reproductive tract disease	i) Ovarian endometriosis ii) Ovarian neoplasms iii) Cervical/uterine neoplasia
Autoimmune conditions	i) Autoimmune oophoritis ii) Treatment of connective tissue disease
Counteract effects of ovarian ageing	'Social' fertility preservation

Reported rates of premature ovarian failure (POF) range from 20–85% with such regimens.[3]

Radiotherapy is significantly toxic to germ cells, with a dose of 5–10 Gy enough to result in ovarian failure.[4] Total body radiotherapy preceding bone marrow transplant carries a particularly high risk of POF. Pregnancy rates following such treatment ranges from 0.6% to 11%.[5–7]

Age and pretreatment ovarian reserve appear to be independent prognostic factors for treatment-related gonadotoxicity. Age-related decline in ovarian reserve leaves older women more susceptible to the gonadotoxic effects of treatment.[8]

Therefore preservation procedures need to be tailored to the individual. Important considerations are the age and pre-existing fertility of the woman, the type of malignancy and treatment planned, the time available for preservation procedures and whether she has a male partner. Prepubescent girls are a particularly challenging group, restricted by limited options, along with ethical considerations pertaining to competence and consent issues.

Fertility preservation associated with genetic conditions

Several genetic mutations are associated with POF. These often affect the X chromosome.[9,10]

Turner syndrome has an established association with POF and infertility. Most women with the disorder undergo ovarian failure at a very young age and many never develop any identifiable ovarian function. A Turner mosaic karyotype increases the possibility of identifying functioning ovarian tissue,[11] which may be amenable to fertility preservation procedures.

Fragile X (FMR1) premutation is also associated with POF. *FMR1* is an unstable CGG triple sequence mutation located on the long arm of the X chromosome (Xq 27.3 locus). Unaffected individuals have 6–50 copies of the CGG repeat. Individuals with repeats in the range of 55–200 copies are carriers of the premutation.[12] Approximately 21% of all premutation carriers develop POF, compared with only 1% of the general population.[12]

Although, in principle, fertility preservation for women with genetic conditions is possible, it is not without controversy. Such women are at risk of resultant aneuploidy in the offspring. While pre-implantation genetic diagnosis may help offset this risk, it does not negate the fact that conditions such as Turner syndrome are associated with medical comorbities that may actually contraindicate pregnancy. Any decision regarding future pregnancy therefore needs to be carefully considered with appropriate counselling.

Fertility preservation for non-malignant disease

Ovarian surgery for benign conditions including endometriosis may diminish ovarian reserve. Several studies report a lower ovarian reserve after ovarian surgery, especially in patients with endometriomas.[13] This may result from incidental incision of normal ovarian tissue during cystectomy or result from damage of healthy ovarian tissue by electrocautery. Fertility preservation procedures should therefore be considered before complex or repeated ovarian surgery in women wishing to conceive in the future.

Patients undergoing chemotherapy or radiotherapy for a variety of non-oncological conditions, including autoimmune connective tissue disease and haematological conditions may also benefit.

Non-medically indicated 'social' fertility preservation

Most recently, 'social' fertility preservation has been assuming increasing importance. In today's society, where increasing professional and financial opportunities are available to women, many are delaying childbearing. Given that female fertility progressively declines with age, delayed childbearing undoubtedly affects a woman's opportunity for pregnancy. With assisted reproduction unable to fully overcome the effect of ageing on fertility loss, fertility preservation is an evolving technology that offers the potential to combat infertility secondary to ovarian ageing.

Options for fertility preservation

Embryo cryopreservation

Embryo cryopreservation is an established method of fertility preservation (Figure 1). Its success and safety is supported by its routine place within in vitro fertilisation (IVF) programmes, where it is commonly used as means of storing surplus embryos after IVF. In addition, interest has

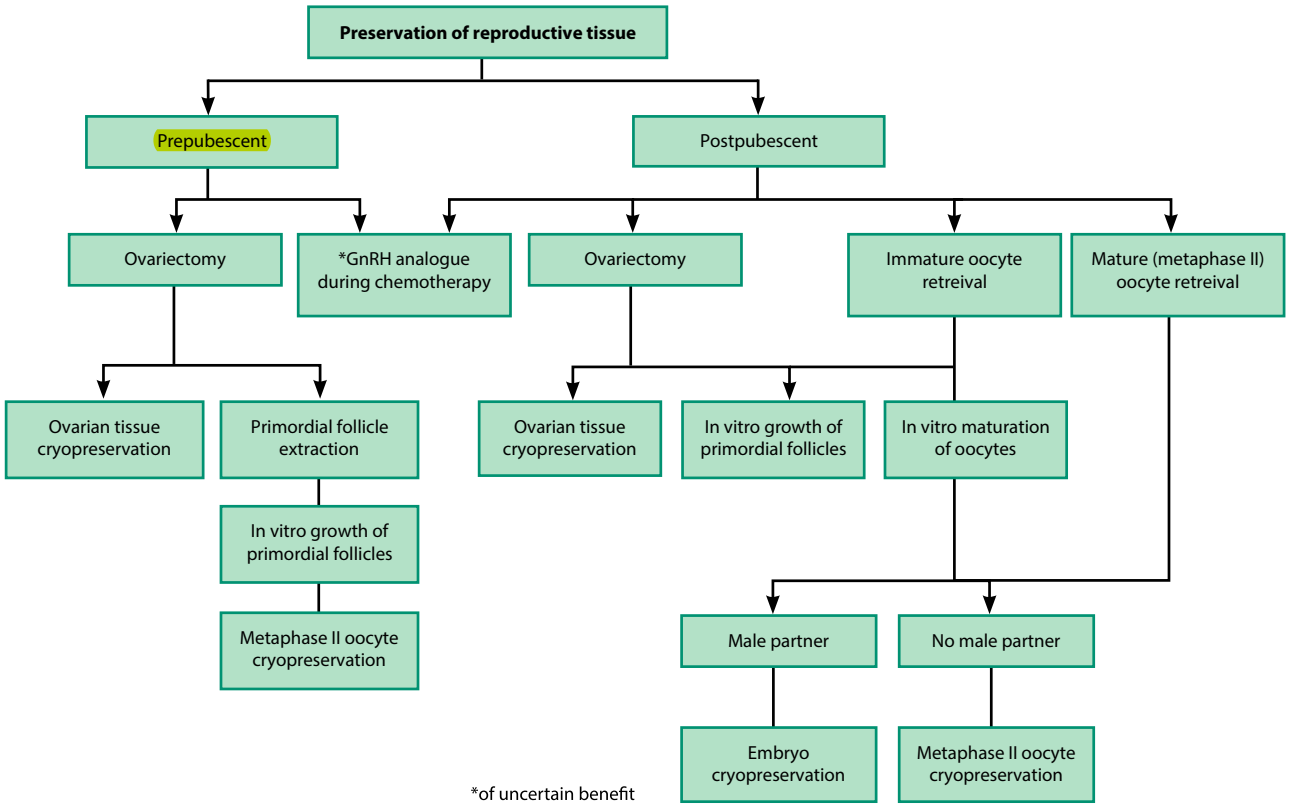

Figure 1. Strategies available to preserve reproductive tissue. GnRH = gonadotrophin-releasing hormone.

recently grown for its application in enhancing standard IVF pregnancy rates through elimination of embryo-endometrium asynchrony and the association with implantation failure.[14] It therefore follows that embryo cryopreservation can indeed provide suitable women needing fertility preservation with a predictable chance of future pregnancy based on the number and quality of embryos preserved. Certainly data from the *American Society for Assisted Reproductive Technologies 2011 National Summary Report*[15] confirm that pregnancy and live birth rates between frozen non-donor embryo transfers and fresh embryo transfers were comparable. Of all non-donor frozen embryo transfers, 44.6% resulted in pregnancy, compared with 43.9% of fresh transfers, with an overall live birth rate of 34.5% for frozen transfers, compared with 35.8% of fresh transfers.[15] The UK Human Fertilisation and Embryology Authority also reports reasonable success rates with frozen embryo transfer, albeit with a slightly lower success rate comparable to fresh transfer. The 2010 data reported pregnancy rates of 23.6% and 34.1% and live birth rates of 19.3% and 25.6% for frozen and fresh transfers respectively. Data from 2011 showed pregnancy rates of 24.7% for frozen and 33.7% for fresh transfers.[16]

Given that embryo cryopreservation requires ovarian stimulation, oocyte retrieval and IVF with the provision of male gametes, women without a male partner who are unwilling to use sperm donation are precluded. Even if sperm donation is considered, it raises additional ethical issues regarding future use. For example, if a woman subsequently has a partner, a decision needs to be made regarding whose gametes to use.

Oocyte cryopreservation

Recent progress with oocyte cryopreservation demonstrates its increasing potential as a viable method of fertility preservation (Figure 1).

Traditional slow freezing initially yielded unacceptably low and inconsistent results. This was attributed to the large water content of the oocyte and the formation of ice crystals during the freezing process damaging the meiotic spindle.[1] Vitrification techniques, however, have dramatically improved results. Indeed, at the end of 2012 the American Society of Reproductive Medicine approved oocyte vitrification for fertility preservation, upholding that it is a safe and effective technique. This introduction into mainstream practice serves to provide women with greater choice and control of future reproductive potential. It provides women without a male partner a viable option of preservation and is also opening up opportunities for non-medically indicated or 'social' fertility preservation aimed at

combatting age-related fertility decline. Further, in contrast to embryo preservation, the use of which requires consent from the storing partner, oocyte cryopreservation allows a woman complete autonomy in her decision-making regarding any future treatment or disposal. It also overcomes religious or ethical objections associated with embryo preservation held by some women.

There is reproducible evidence that oocytes vitrified in the second phase of meiotic division are able to survive the vitrification and warming process. Documented survival rates range from 74.5% to 96.9%.[17–24] It is also encouraging to note that when comparing 'fresh' oocytes with vitrified oocytes, there does not appear to be any demonstrable difference between fertilisation, cleavage or blastocyst formation rates.[17,19,21] Notably, pregnancy success rates following the use of vitrified oocytes have been reported as comparable with those using 'fresh' oocytes, without any increased risk of aneuploidy or congenital anomalies.[20,22] Indeed, increasing numbers of successful pregnancies are being achieved following oocyte vitrification.[23]

Given that there is a progressive loss of both oocyte quality and quantity associated with female ageing, the success associated with this technology is undoubtedly influenced by the age of the woman at the time of preservation. Rienzi et al.[23] report dramatically diminished results in women >38 years of age, with each year of maternal age decreasing the delivery rate by 7%. As such, women interested in preserving fertility to counteract future ovarian ageing need to be informed that the chances of success are likely to improve when oocytes are harvested and cryopreserved at a younger age, when oocyte quality is better.

Prepubescent girls are unfortunately precluded from ovarian hyperstimulation. This is not only due to inherent difficulties with stimulation on immature ovaries, but also due to an inability to perform standard transvaginal follicular tracking or oocyte retrieval procedures in such a population. Postpubescent girls who have not yet become sexually active may also be unsuitable for transvaginal procedures, although consideration may be given to transabdominal tracking and laparoscopic oocyte retrieval.

Modified ovarian stimulation for women with malignancy

Following a diagnosis of cancer, it is extremely important that any oncological treatment is undertaken in a timely manner.

If ovarian stimulation is required, the general recommendation is for a single cycle, although multiple cycles may be considered in individual circumstances, particularly if response to stimulation is low. If conventional stimulation is undertaken, short gonadotrophin-releasing hormone (GnRH) antagonist cycles are preferred to down regulation cycles, facilitating oocyte retrieval in the shortest space of time, generally within 2 weeks.

Ovarian stimulation is conventionally initiated at the beginning of the follicular phase, with the assumption that this optimizes clinical outcome. Adhering to this protocol may result in either an unacceptable delay in commencing oncological treatment or even necessitate foregoing fertility preservation altogether. 'Random-start' cycles have been introduced as alternative, emergency measures. Reassuringly, they do not appear to be any less effective than conventional cycles.[25] There are several strategies for 'random-start' stimulation as highlighted in Figure 2.

Ovarian stimulation is associated with supraphysiological levels of circulating estradiol produced from the maturing follicles. This theoretically poses a risk to women with estrogen sensitive malignancy, such as breast or endometrial cancer. Given this potential risk, modified stimulation protocols using aromatase inhibitors or tamoxifen have been introduced.[26]

Aromatase inhibitors markedly suppress plasma estrogen levels by competitively inhibiting the activity of the aromatase enzyme, which catalyses the conversion of androstenedione and testosterone to estrone and estradiol.[27] The consequent hypoestrogenic state creates an endogenous discharge of follicle-stimulating hormone (FSH) through negative feedback mechanisms. Oktay et al.[28] found that in comparison with age matched controls undergoing IVF for tubal factor, ovarian stimulation combined with the aromatase inhibitor letrozole demonstrated a significant lowering of peak estradiol levels, along with 44% decrease in gonadotrophin requirement without affecting oocyte or embryo yield. Moreover, in patients whose stimulation protocols use letrozole as an estrogen lowering adjunct, recurrence rates for breast cancer were reassuringly not increased at 2-year follow–up.[29] Letrozole has also been safely used for embryo cryopreservation in endometrial cancer patients.[30]

The selective estrogen receptor modulator tamoxifen is an alternative for ovarian stimulation in patients with breast cancer. Due to its anti-estrogenic effects on breast tissue, it is commonly used as a breast cancer treatment. Additionally, being a non-steroidal triphenylethylene compound related to clomiphene, it has also been effectively used for ovulation induction and controlled ovarian stimulation.[31] Selective competitive antagonist action within the CNS creates a perceived hypoestrogenic state, which through negative feedback mechanisms stimulates release of endogenous FSH. As such, tamoxifen has the potential to create a clomiphene-like ovarian response, while at the same time maintaining anti-estrogenic effects on breast tissue. While peak estradiol levels are not altered, its anti-estrogenic effect on the breast helps to offset this risk, with no evidence of recurrence compared with unstimulated controls.[32]

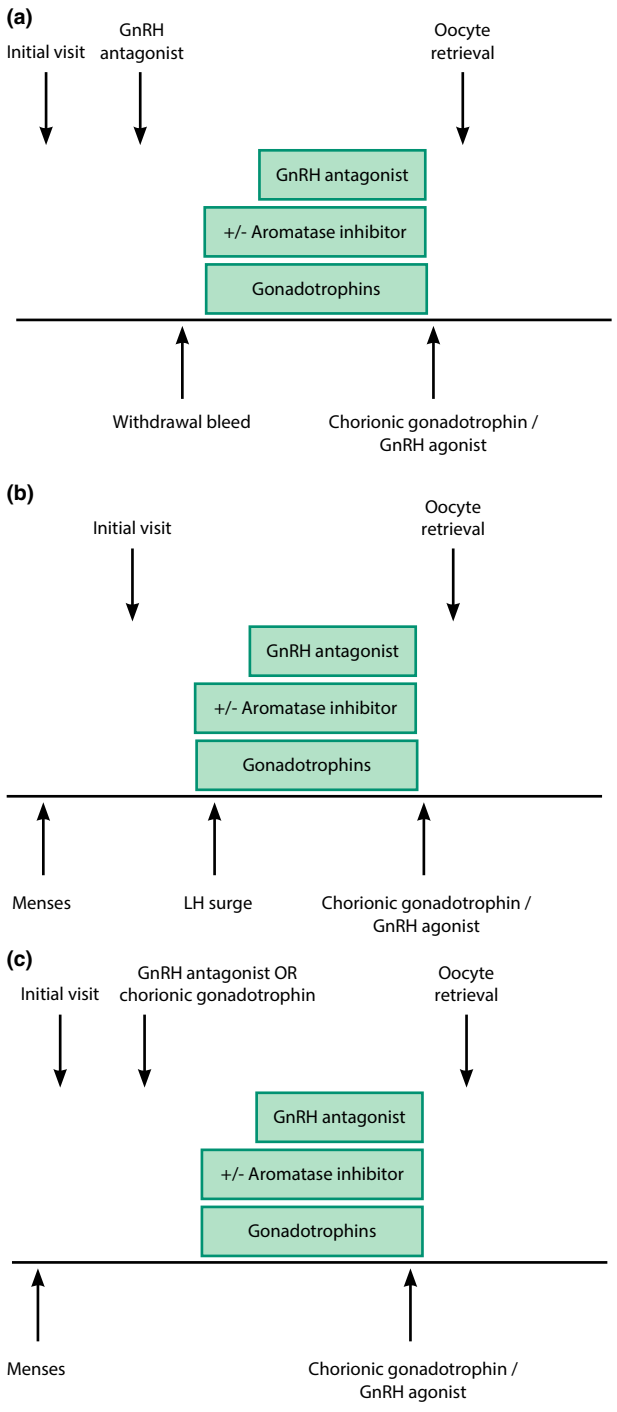

Figure 2. 'Random start' ovarian stimulation[19] (a) Luteal phase presentation with accelerated luteolysis: menses brought forward by accelerating luteolysis with administration of gonadotrophin-releasing hormone (GnRH) antagonist, following which a conventional start protocol may be followed (b) Late follicular phase presentation with lead follicle <12 mm: immediate stimulation without GnRH antagonist commenced. After endogenous LH surge, GnRH antagonist is introduced once secondary follicle cohort reaches 12 mm, preventing a premature secondary LH surge (c) Late follicular presentation with lead follicle exceeding 12 mm: ovulation induced with chorionic gonadotrophin or GnRH agonist, followed by stimulation 2–3 days later.

In vitro maturation of immature oocytes

In vitro maturation of immature oocytes (IVM) refers to the process of retrieving immature oocytes from ovarian antral follicles, followed by in vitro maturation (Figure 1). The process involves minimal or no gonadotrophin stimulation. Avoiding any significant ovarian stimulation not only negates the risks associated with supraphysiological circulating estrogen, but also allows retrieval of oocytes in a timely manner, avoiding the delay that stimulation incurs.

The main focus with IVM has predominately been as an alternative treatment option for women with polycystic ovaries at increased risk of ovarian hyperstimulation syndrome (OHSS). Success, however, has also been reported in women with morphologically normal ovaries, allowing wider application.[33]

In vitro maturation rates following 48 hours in culture have been reported to range from 62.2% to 85.2%, with subsequent fertilisation rates ranging from 61% to 90.7%.[34–36] It is also encouraging to note that successful pregnancies and live births have resulted without increased incidence of perinatal problems.[37]

Given that increasing numbers of antral follicles increase the chance of obtaining a good yield of oocytes, one needs to consider that any application must take into account that antral follicle count and ovarian reserve are significant prognostic factors for success.

Ovarian tissue cryopreservation

Ovarian tissue cryopreservation is an experimental technology involving the harvest and cryopreservation of ovarian tissue (Figure 1). It is usually performed with the aim of preserving reproductive potential prior to gonadotoxic medical treatments. On completion of gonadotoxic treatment and confirmed fitness for pregnancy, the harvested autologous tissue may be transplanted back to the patient.

Although several successful live births have been reported after such technology,[38] given its experimental nature, along with tissue storage regulations in the UK, its use is currently limited. In addition, there are concerns regarding the risk of malignancy from the transplanted tissue. Histological examination of the tissue prior to transplantation is warranted, but cannot guarantee the absence of cancer cells. Nonetheless, it is the only cryopreservation method available for prepubertal girls and is a possible alternative for women not willing to undergo ovarian stimulation or oocyte retrieval.

Ovarian tissue containing primordial follicles is harvested, cryopreserved and then transplanted at a later date. The usual technique is to harvest ovarian cortex, which is cut into thin strips of tissue, typically 0.3–2 mm thick, which are then cryopreserved.[39] Primordial follicles have been shown to effectively tolerate cryopreservation, although initial ischaemia encountered after transplantation destroys a significant proportion of these available follicles.[40] This necessitates the need to preserve a large volume of ovarian cortex to ensure adequate follicle numbers and also limits the technique to younger women with good ovarian reserve. Whole ovary cryopreservation with an intact vascular pedicle has also been proposed, with the intended benefit of improved post-transplant blood flow and reduced risk of tissue ischaemia.[41]

Cryopreservation of ovarian tissue has traditionally used slow freezing. The possibility of vitrification however has recently gained popularity following good results with oocyte and embryo vitrification. Recent research is certainly showing promise. Silber et al.[42] reviewed the survival of oocytes after enzymatic isolation from ovarian tissue following cryopreservation by vitrification or slow freezing and found an 89.1% oocyte survival rate for the vitrified ovarian tissue compared with 41.7% for the slow frozen tissue.

Ovarian tissue transplantation

While ovarian tissue transplantation is primarily indicated for the autologous transplantation of previously cryopreserved tissue, the experimental technology has been broadened to include allotransplantation.[43,44]

For women with ovarian failure, while oocyte donation and IVF is the current method of providing reproductive capacity, ovarian allotransplantation is evolving as a potentially useful alternative, particularly in cases of repeated failure with oocyte donation or in cases where the ethical or religious morals of the patient preclude IVF. Indeed, successful pregnancies have been achieved through allotransplantation between monozygotic twins discordant for ovarian failure.[44]

The transplantation may be orthotopic, whereby the tissue is placed onto the remaining ovary or into a peritoneal pocket within the pelvic peritoneum or ovarian fossa. Alternatively it may be heterotopic, being placed outside the peritoneal cavity. Chosen heterotopic sites include the abdominal wall, forearm and chest.[45]

Orthotopic transplantation has the advantage of potentially allowing natural conception and indeed is the method with the most success. A recent review report confirms 24 live births worldwide using this technique.[38] Heterotopic transplantation has achieved less success, with no published successful pregnancies to date, however, there are documented reports of restoration of hormonal function, follicle development and oocyte retrieval from such sites.[46,47] The lower overall success is postulated to be a result of a less favorable environment for follicular development, with differences in temperature, pressure, vascular supply and paracrine effects coming into play.[48]

The return of ovarian function following transplantation depends on a variety of factors. These include the freezing protocol, baseline ovarian reserve, vascularisation of the graft, site of the graft, plus ischaemia time after thawing prior to transplantation.[48] Many studies have shown that ovarian function returns after 12–18 weeks following heterotopic transplantation and 8–18 weeks after orthotopic transplantation.[49–51]

While success has been reported with ovarian tissue cryopreservation, it is important that any women (or parents) wishing to consider such technology are made aware of its experimental nature and a lack of guarantee regarding future pregnancy.

Ovarian suppression during gonadotoxic chemotherapy

It has been hypothesised that concomitant use of GnRH analogues alongside chemotherapy may protect ovarian follicles from chemotherapeutic damage (Figure 1). The basis of this hypothesis stems from the theory that if gonadotrophins are suppressed then this should prevent primordial follicle recruitment. Unfortunately, while the full physiology of primordial follicle development is not fully appreciated, it is understood that primordial follicles actually lack FSH receptors and initial recruitment is therefore independent of gonadotrophins.[52] This brings into question the validity of any such hypothesis. Certainly, studies to date have yielded insufficient evidence. In addition, safety concerns have been raised, specifically concerning the possibility that concomitant use of GnRH analogue treatment during chemotherapy may actually dampen the chemotherapeutic response in those with hormonally sensitive malignancies. Many of these malignancies actually express GnRH receptors that mediate various effects including inhibition of proliferation, induction of cell cycle arrest and inhibition of apoptosis induced by cytotoxic drugs.[52]

Any woman interested in ovarian suppression should be fully counselled regarding the lack of robust data and safety and it should only be carried out within the context of a clinical trial.

Ovarian transposition

Ovarian transposition is a surgical procedure performed prior to pelvic radiotherapy. It involves removing the ovaries from the pelvis and placing them away from the planned radiation field. The procedure may be performed at laparotomy, laparoscopy or via robotic surgery. Unlike laparotomy, laparoscopic transposition does not require

significant incisional healing time, providing the advantage of being performed immediately prior to radiotherapy.

Transposition following division of the ovarian ligament is the preferred method, with the recommendation that repositioning is at least 3 cm above the upper border of the radiation field.[53] The procedure should be performed in close timing to radiotherapy due to the possibility of ovarian remigration. Metallic clips can be used for fixation to allow easy identification on the pre-radiation film.

Evidence of efficacy of ovarian transposition is limited. Small studies and case reports have, however, suggested benefit. A study by Barahmeh et al.[54] demonstrated ongoing ovarian function in 87.7% of adult women at 42-month follow-up. Failures are attributed to scatter radiation and alteration in ovarian blood supply.

Any discussions regarding ovarian transposition also need to highlight that radiotherapy may actually impair uterine function,[55] and therefore, regardless of ovarian function, risks affecting the woman's ability to carry a pregnancy, unless it is with the assistance of a surrogate.

Fertility sparing surgery

Gynaecological malignancy poses a threat to reproductive function. While loss of fertility may be a necessity for a proportion of women, surgical preservation techniques are becoming increasingly achievable.

Traditionally, cervical cancer was treated via radical hysterectomy. Today many women with very early stage disease are amenable to fertility preserving treatments. Women with stage 1A1 disease can be treated with isolated local excision via LLETZ or cone biopsy and women with 1A2 and small stage 1B1 disease (tumour size <2 cm) may be treated via trachelectomy. Simple trachelectomy may be sufficient for 1A2 disease and radical trachelectomy an option for those with small 1B1 disease. Vaginal, laparoscopic and robotic techniques are possible and successful obstetric outcomes have been achieved without compromising oncological outcomes.[56]

As with cervical cancer, the treatment of ovarian cancer is evolving to include conservative strategies with reasonable success. Unilateral salpingo-oophorectomy may be considered over traditional primary surgical staging in women with well differentiated 1A and 1B disease.

New frontiers

For women who possess ovarian tissue but lack a functioning uterus, either as a consequence of congenital absence, previous hysterectomy or severe and untreatable intrauterine adhesions, surrogacy is currently the only accepted method of achieving pregnancy. Unfortunately, surrogacy is banned in many countries due to ethical, legal or religious reasons. An experimental trial is, however, well underway assessing the possibility of uterine transplantation. The team, headed by Brännström has already demonstrated that, not only is uterine transplantation possible, but the ultimate outcome of a healthy live birth has been achieved from a transplanted uterus.[57] While such transplantation is still very much in its infancy, with a need for greater understanding of both the medical and psychological risks involved, this achievement, nonetheless, truly takes reproductive medicine into a new frontier and helps to facilitate the possibility of childbearing for women with absolute uterine factor infertility.

As with any transplantation, immunosuppression is necessary to prevent organ rejection and maintain graft survival. It is well known that immunosuppressed transplant patients are at increased risk of infectious diseases and malignancy.[58,59] While the aetiology of post-transplant malignancy is believed to be multifactorial, it is recognised that suppressed antiviral immune activity may play a significant role, particularly in cases of viral related malignancy such as human papillomavirus (HPV) associated cancers. It is therefore a concern that patients with a prior history of malignancy, particularly HPV-related cervical cancer, may be at increased risk of recurrence with immunosuppression.[57] While the risk of recurrent or de novo malignancy does exist following transplantation, it does not preclude cancer survivors from uterine transplantation and, indeed, current trial participants have included those with a prior history of cervical cancer. The following have been highlighted by Brännström and his team in relation to uterine transplantation and the risk of malignancy:[60] first, uterine transplantation is ephemeral, minimising the risks associated with long-term immunosuppression; second, it is well documented that the progression of HPV infection to cancer is slow, and this is confirmed by longitudinal epidemiological studies,[61,62] making the risk of HPV-related malignancy in uterine transplantation extremely unlikely; third, any cancer patients would be expected to have a minimum disease-free period of 5 years prior to transplant. It is also a requirement that all the transplant patients, their partners and the donors are HPV negative at baseline testing. The trial protocol has also recently been extended to incorporate HPV vaccination to all involved, regardless of previous HPV status.[60]

The results thus far are very promising. It now appears that the biggest challenge to the success of uterine transplantation going forward is more likely to result from ethical issues surrounding the treatment, rather than due to the limitations of medicine.

Conclusion

The ability to bear children is, for many, of great importance. Profound psychological sequelae are prevalent among those

unable to bear their own offspring. Certainly advances in fertility preservation help to reduce this burden, but at what cost? Individuals are subjected to invasive procedures, without an absolute guarantee of future pregnancy. In particular, are such procedures acceptable in women already affected by a diagnosis of cancer, and do these treatments risk adversely affecting oncological outcomes?

The introduction of 'social' fertility preservation requires a woman to make a significant financial investment in a process, of which the benefit is uncertain. It also subjects healthy women to procedures with medical risks that could jeopardise future fertility. It also potentially encourages women to delay childbearing.

With childbearing at later maternal age increasing the risk of medical and obstetric complications, are these advances simply adding a new medical burden to society? Increasing social awareness of age-related decline in fertility may actually be a more productive means of combating the issue. It should also be noted that, with 'social' fertility preservation still in its infancy, the full impact of such interventions has yet to be determined. Nonetheless, with documented success already achieved in the assisted reproduction population, including that of healthy donors, extrapolation of these results is not unreasonable.

The recent progress made with uterine transplantation is exciting, but with the experimental technique in its infancy, we have a lot to learn, particularly regarding the long-term health of both the recipient and their offspring.

Finally, any woman contemplating fertility preservation should be offered additional specialist services. In particular, given any treatment is likely to be both physically and emotionally stressful, psychological and counselling services should be made available to provide additional support throughout the treatment process.

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