Preservation of fertility in adults and children diagnosed with cancer

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In the United Kingdom each year 11,000 patients aged 15-40 years are diagnosed with cancer, and more than half of them will live for more than five years. Patients want quality of life, including the ability to have a family, and many request advice on fertility preservation. This review describes the fertility preservation techniques available and recent recommendations from the UK and the United States.

Why should oncology patients consider fertility preservation?
Chemotherapy and radiotherapy reduce the number of germ cells within the ovary and decrease testicular spermatogenesis; this reduction is related to the dose, agent used, and age at treatment. In addition, patients are at risk of permanent gonadal failure. The persistence of menstrual cycles after treatment does not preclude ovarian damage, and the preservation of testosterone production does not confirm the preservation of spermatogenesis.

Who should be referred to discuss fertility preservation options?
UK and American Society of Clinical Oncology (ASCO) guidelines recommend that the implications of oncological treatment for fertility are discussed with patients. The need to refer for fertility advice will depend on the patient’s age, disease, prognosis, and time interval before treatment. Many patients seek advice from their general practitioner, oncologist, and allied health professionals, but evidence from several observational studies indicates that many do not receive adequate informed advice.

What options are available for men?
As a result of the systemic effects of cancer, semen quality is often poor, and azoospermia is often present in Hodgkin’s lymphoma and testicular cancer before chemotherapy. The sperm count is lowest in the six months after treatment and may need two years to recover. The risk of producing chromosomally abnormal sperm is highest in the few weeks after completion of chemotherapy, so men should wait six months before conception is attempted. Hormonal suppression has not been shown to help reduce testicular damage caused by chemotherapy.

Men and adolescent boys preparing for chemotherapy should be offered semen cryostorage, which has been shown to be effective in many small observational studies and is recommended by the National Institute for Health and Clinical Excellence (NICE) and ASCO. Large prospective studies have found no increase in abnormalities for children born after semen cryopreservation, although sperm that have been frozen may be less effective in assisted reproduction. It is difficult to discuss the production of semen samples with adolescent boys and we have no reliable method to determine if they are able to produce a sample. Anecdotal evidence suggests that for boys who are unable to ejaculate, taking a urine sample after masturbation may help isolate some sperm.

What options are available for women?
Women in a committed relationship
After chemotherapy the ovary is at risk of permanent gonadal failure, and sensitivity to chemotherapy increases with age. Exposing the ovary to gonadotoxic agents accelerates the age related decline in oocyte number. Women treated with chemotherapy may have premature ovarian failure and may experience the systemic effects of oestrogen deficiency; including osteoporosis, and the psychological impact of a premature menopause, according to the agents used and the duration of treatment.

If sufficient time exists before the woman starts chemotherapy or radiotherapy, she could undergo in vitro fertilisation (IVF) to cryopreserve embryos, providing she has a normal platelet count and can...
tolerate the anaesthesia needed for oocyte retrieval. As with any IVF cycle, too few oocytes may be collected or the cycle may have to be cancelled because of the risk of hyperstimulation syndrome. This is always distressing, but if this is the woman’s only chance of preserving her fertility, it is devastating. Any resulting embryos will be cryopreserved and when required single embryos can be thawed and replaced in the uterus. However, only about 15% of thawed embryos result in a live birth.15

Is IVF safe in women with oestrogen receptor positive breast cancer?

In women with oestrogen receptor positive breast cancer, the raised oestrogen concentrations generated by IVF could accelerate the disease process, although this has yet to be confirmed by prospective studies.10 Performing ovarian stimulation with concurrent administration of an aromatase inhibitor or tamoxifen may temper this effect. This approach was used in a study of more than 100 patients who were prospectively compared with patients not undergoing fertility preservation. It did not interfere with the IVF cycle and recurrence was not increased.17 A technique that avoids ovarian stimulation—whereby immature oocytes are collected and matured by in vitro maturation—has been used successfully in some women with polycystic ovary syndrome.19 This technique might be useful in women with oestrogen receptor positive breast cancer.

After diagnosis women are generally advised not to try to conceive for up to five years because they are taking adjuvant hormonal therapy, although observational evidence derived from large cohorts suggests that conceiving within two years of treatment does not influence survival.20

Several retrospective studies and one recent randomised controlled trial of 80 patients showed that suppressing ovarian activity—with a gonadotrophin hormone releasing agonist, for up to six months concurrent with chemotherapy helped preserve ovarian function—although the evidence was not conclusive.3 22-24

What options are available for single women?

Freezing oocytes

Single women, or women not in a stable relationship, cannot usually cryopreserve embryos because they must be sure that a partner would give permission for their future use. Such women can start an IVF cycle and freeze any oocytes collected, without having them fertilised. However, systematic reviews show that, despite advances in freezing techniques, for each oocyte retrieved the chance of a live birth is only 3-5%.25 26 Expert consensus is that this technique is developmental and should not be considered routine; consequently, it is not funded by the NHS.14

Alternative strategies for single women, women with insufficient time for embryo cryopreservation, or women who are unable to countenance the further emotional or financial burden of IVF at this difficult time include freezing ovarian tissue or adopting a “wait and see” policy and relying on receiving donated oocytes if unable to conceive in the future.

Oocyte donation

Oocyte donation is a well established form of assisted reproduction—20% of embryos replaced result in a live birth (data derived from national registries).15 Small observational studies show that both parents bond as well with their child as those couples who conceive spontaneously.27

Harvesting and freezing ovarian tissue

The process of harvesting ovarian tissue is less well established and still at the developmental stage.4 Ovarian cortex is removed during laparoscopy and cryopreserved for potential reimplantation at a later date. Storage of such tissue in the UK is subject to tissue banking regulations (www.sba.gov.uk), and its availability is therefore very restricted, whereas sperm, eggs, and embryos are stored and used in a licensed centre...
What are the effects of pelvic irradiation for women?

Uterine effects

Pelvic irradiation may lead to myometrial fibrosis and poor endometrial development. Small observational studies indicate an increased risk of miscarriage, growth restriction, and premature delivery depending upon the site, dose, and duration of treatment.34 35 In one study of 33 infants born to women after abdominal irradiation, 10 weighed less than 2500 g and three died during the perinatal period.35 Furthermore, the prepubertal uterus is thought to be more vulnerable to radiotherapy than the mature one, so radiotherapy might cause irreparable impairment of uterine growth.34 36 37

Ovarian failure

Patients undergoing pelvic irradiation should be warned of the gonadotoxic effect of radiation, which accelerates the natural process of ovarian ageing.34 Radiotherapists can predict the likelihood of ovarian failure by using a modified model of natural oocyte decline.38 Performing laparoscopic ovarian transposition—by moving the ovary on its vascular pedicle laterally from the incident radiation—can minimise exposure to ionising radiation and reduces incident pelvic radiation, according to the site of treatment and the distance the ovary is moved.39 Subsequent spontaneous conception may occur, but if IVF is needed the ovaries may require repositioning to enable vaginal access, or the patient may need to undergo laparoscopic egg collection.

What are the effects of cranial irradiation?

Cranial irradiation may initiate hypogonadotrophic hypogonadism. If this occurs, ovulation or spermatogenesis will need to be induced with both exogenous follicle stimulating hormone and luteinising hormone or human chorionic gonadotrophin.

What options are available for children and adolescents?

Children pose a difficult ethical problem because although they may have some insight into the potential effect of their cancer treatment on their fertility, it is usually their parents who are more worried about preserving reproductive function. The prepubertal testicle is more vulnerable to the cytotoxic effects of chemotherapy than the adult testicle.7 As described, adolescent boys may be able to store a semen sample, but those who cannot produce one by masturbation may find that penile vibratory stimulation is more successful. Ethical board approval may be needed before considering surgery for testicular extraction of sperm in an adolescent boy. The retrieval of precursors of spermatozoa or spermatogonial stem cells for subsequent reimplantation or in vitro maturation for use in IVF has not been used in prepubertal boys, although it has been successful in animal models.7 The production of testosterone by Leydig cells can be preserved after chemotherapy, and in such cases normal pubertal progression would be expected.7 The prepubertal and early adolescent ovary is less vulnerable to the effects of chemotherapy and radiotherapy than the mature ovary. None the less, after counselling, girls undergoing radiotherapy or chemotherapy may be considered for ovarian tissue harvesting—a hospital ethics committee should help with such decisions.40

How should a doctor discuss these effects with a patient?

Observational studies indicate that, despite most patients’ desire to be informed about the effects of

Additional educational resources

Resources for healthcare professionals


American Society of Clinical Oncology. Recommendations on fertility preservation in cancer patients. http://jco.ascopubs.org/cgi/content/full/24/18/2917


Human Fertilisation and Embryology Authority (www.hfea.gov.uk)—The UK’s independent regulator overseeing the use of gametes and embryos in fertility treatment and research

Resources for patients


SUMMARY POINTS

- Warn patients of the possible effects that treatment may have on their reproductive capacity
- Provide access to a fertility specialist and supportive counselling
- Sperm banking is an effective and well-established technique for adolescent boys and men
- Women should be offered access to oocyte or embryo freezing if sufficient time is available before treatment begins
- Oocyte cryostorage has limited success before treatment begins

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cancer treatment on their fertility; 1 many doctors and family members tend to focus on the immediate treatment of a patient with a life threatening illness, 2 and only a minority of patients receive this advice. 3, 4

The implications of a patient’s treatment on their fertility will depend on the patient’s age, understanding, the type of cancer, and treatment. Any doctor-patient discussion will be influenced by the wishes of a partner if the patient is in a relationship. The chance of a live birth is substantially better for a woman who freezes embryos than for one who freezes unfertilised eggs. A woman may have to make a difficult decision about the strength of a current relationship as she tries to decide whether to freeze embryos or eggs, set against a background state of distress due to a recent diagnosis of cancer, the threat of chemotherapy and possible menopause. Supportive counselling by a trained fertility counsellor is therefore essential. 5, 6

In the UK, IVF treatment cannot be offered to a couple unless it is in the best interests of the child born from the treatment. Consequently the treating IVF clinician and counselling staff should take a broad view before starting treatment. Thanks to Martha Hickey for her comments and suggestions in preparing this manuscript.

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