*BMJ* 2016;355:i6145 doi: 10.1136/bmj.i6145 (Published 30 November 2016) 

EDITORIALS

# Preserving fertility in girls and young women with cancer

Awareness of and access to services remains poor in the UK

Richard A Anderson *professor of clinical reproductive science*[1], Melanie C Davies *consultant gynaecologist*[2]

[1]MRC Centre for Reproductive Health, Queens Medical Research Institute, University of Edinburgh, Edinburgh, UK; [2]Reproductive Medicine Unit, Department of Women's Health, University College London Hospitals, London NW1 2PG, UK

Advances in the treatment of cancer in children and young adults have meant that more survivors are living with the long term consequences of treatment.[1] Loss of fertility is a big concern,[2] and infertility is common after high dose chemotherapy and pelvic irradiation.[3] Fertility preservation has been available to men for many years; semen cryostorage before treatment yields viable sperm for later in vitro fertilisation (IVF). Women, however, require more complex and invasive procedures.[4] This aspect of the holistic care of young people with cancer has been highlighted by the recent announcement of the first baby born in the UK to a woman who had regrafting of ovarian tissue that was cryopreserved 10 years earlier.[5]

The options for women facing loss of fertility from treatment for cancer or other therapies include cryopreservation of oocytes, embryos, or, more experimentally, ovarian tissue. Embryo freezing has been used successfully for three decades. Oocyte freezing is technically more challenging, although the development of vitrification (a technique that prevents ice crystals forming), has greatly improved pregnancy rates.[6] This is now a viable option for single women, who retain sole control over future use, whereas embryos are the joint property of the man and woman who contributed gametes. Cryopreservation of both oocytes and embryos requires ovarian stimulation and egg retrieval, which takes two to three weeks and introduces potential delays in cancer treatment. The high oestradiol concentrations induced during stimulation and retrieval add extra risk for women with hormone sensitive cancers.[7]

Cryopreservation of ovarian tissue requires a laparoscopic surgical procedure and thus, although more invasive with a small risk of surgical complications, can be carried out more quickly. Subsequent re-implantation of ovarian tissue can restore fertility (success rates are around 20%),[8] with the additional benefit of oestrogen production, although it carries a risk of re-implantation of malignancy if the cryopreserved tissue contains micrometastases.[9] Cryopreservation of ovarian tissue is still widely viewed as experimental, particularly for pre-pubertal girls.[3]

The National Institute for Health and Care Excellence (NICE) guidelines on fertility recommend offering oocyte or embryo cryopreservation to women of reproductive age (including adolescent girls) before cancer treatment that is likely to make them infertile provided that they are well enough, it will not worsen their condition, and enough time is available.[10] Fertility preservation may also be valuable in non-malignant diseases for which treatment carries a high risk of loss of fertility—for example, bone marrow transplantation for sickle cell disease.

Access to fertility preservation varies widely internationally, and the choice of technique differs according to national legislation, regulation, and local practice.[11] Provision is particularly haphazard across the UK. Despite the NICE recommendations, there are substantial obstacles in terms of access and funding. Patients may not know that fertility preservation is possible because awareness among oncologists is variable and referral pathways are often lacking. Oocyte storage is not yet available in all IVF laboratories, and storage of ovarian tissue remains very limited in the UK, although there are good examples of national networks in Europe.[8] In some areas, NHS funding is taken from infertility services; in others funding is requested from commissioners on a case-by-case basis. Funding from oncology budgets has been proposed, as it is argued that fertility preservation is part of the patient's cancer care. Patients' eligibility for fertility preservation may also be subject to access criteria for infertility treatment—for example, exclusion of women who already have children, have a high body mass index, or who smoke.

The chance of successful birth after fertility preservation in women who have survived cancer is unclear, and the evidence is dominated by small case series.[8] Fertility outcomes from cryostorage require long term follow-up, currently absent from most studies. The highly regulated assisted reproduction sector already records information that could be enhanced and used more effectively—for example, UK data collection does not include the reason for oocyte cryopreservation. We do not know

Correspondence to: M C Davies Melanie.Davies@uclh.nhs.uk

how many women are undergoing fertility preservation or how many women with stored oocytes or embryos actually use them.

Finally, evidence based criteria for access could identify those women at high risk of infertility and those who can be reassured that their risk is low,[12] minimising unnecessary interventions and storage of reproductive samples that will not be used. These data are important to assess the efficacy and cost effectiveness of fertility preservation in women and girls with cancer.

Fertility preservation is an emerging medical specialty that straddles oncology and infertility care but requires specialist services in its own right. Better routine data collection is essential, along with good trials, to determine the efficacy of treatment and give girls and women a fully informed choice. There is an urgent need to improve information for patients, education for oncologists, and equity of funding, to overcome the barriers to more widespread use of fertility preservation in the UK.

Competing interests: Both authors have read and understood BMJ policy on declaration of interests and have no relevant interests.

Provenance and peer review: Not commissioned; externally peer reviewed.

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