The effects of cancer treatment on reproductive functions

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Approximately 11,000 adults in the age group 15–40 years are diagnosed with cancer each year in the UK. Although treatment and, where possible, cure are of paramount importance, the psychological effects of subsequent impairment of fertility or reproductive function, if this occurs, should not be underestimated. Remarkable advances have occurred in the management of cancer in the last 20 years with a marked increase in cure rates. This has been achieved at the expense of increasing exposure of these patients to treatment (eg adjuvant chemotherapy for breast cancer) and potentially gonadal toxicity. Meanwhile, very limited or no data are available on the risks of newer drugs, small molecules or antibodies in terms of gonadal toxicity.

In a new intercollegiate report, representatives from the Royal Colleges of Physicians, Radiologists (RCR) and Obstetricians and Gynaecologists (RCOG) have combined to consider this important topic and make recommendations about patient management and funding of fertility services.[1] The report incorporates sections on normal human reproductive physiology and the effects on this of chemotherapy and radiotherapy, with particular emphasis on those cancers which occur most commonly in young adults. The prevention and management of treatment-related gonadal toxicity are described in detail.

What can be done to ameliorate these problems?

Treatment technique can be important. For radiotherapy, this predominantly comprises attempts to physically remove the gonads from the treatment field (eg oophoropexy) or the use of blocks to shield them. Surgically a developmental technique in early stage cervical cancer is the use of trachelectomy – removal of the malignant cervix only, avoiding hysterectomy or irradiation. For chemotherapy, the options are more limited. However, the increasingly widespread use of adriamycin, bleomycin, vinblastine and dacarbazine (ABVD) for Hodgkin's disease, which is minimally gonadotoxic when compared with older alkylating agent based regimens, is a good example of a definite advance. Where the possibility of gonadal toxicity remains, attempts to conserve fertility should be put in place.

For the male, sperm banking is a well validated, widely available technology with good success rates. This should be initiated prior to treatment likely to affect fertility. Sperm of almost any quantity or quality should be stored, as intracytoplasmic sperm injection (ICSI) is a highly successful *in vitro* fertilisation (IVF) technique. If no sperm are present in the ejaculate then sperm can sometimes be obtained from the testis (testicular sperm retrieval) even in the presence of azoospermia.

The management approaches available to females are more difficult, time consuming (and may be inappropriate for some malignancies) and expensive. The best validated technique, for which a partner or sperm are required, is egg retrieval, IVF and embryo storage, with good success rates at reimplantation. New and developmental techniques (not currently funded in the NHS) include egg retrieval and storage, and storage of ovarian strips with a view to subsequent reimplantation and egg retrieval. These techniques should be regarded as developmental with a very low chance of subsequent successful pregnancy for egg storage, and only anecdotal reports of success following ovarian strip storage.

A common complication of anti-cancer treatment in females is premature menopause. It is essential that hormone replacement treatment be initiated and continued until the normal age of menopause in these women as otherwise osteoporosis may result. Similar problems may occur in males, particularly in the context of testicular cancer, and testosterone replacement should then be lifelong.

A further important issue is patient information. The report strongly advocates full discussion of the potential for gonadal toxicity with patients and their

relatives, with written documentation of these discussions in the clinical notes. Wherever possible independent psychosocial support should be available. Included within this report are patient information leaflets for males and females which have been jointly written with Cancerbackup, and approved by RCR and RCOG.

The preceding paragraphs describe an optimal approach to patients undergoing treatment which may cause gonadal toxicity. These recommendations were supported in a National Institute for Clinical Excellence report published in February 2004 but unfortunately no funding streams were identified at that time.[2] In practice, there are major funding problems in the UK. While sperm banking is often (although not always) funded, as is urgent embryo storage, this is certainly not the case for testicular sperm retrieval and egg or ovarian strip storage. These latter techniques may be commercially available, but uncontrolled developments of this sort are undesirable, and unlikely to advance the state of the art. Unfortunately, even when gamete retrieval and storage are funded manipulation of the gametes (eg artificial insemination using partner's sperm or IVF) may not be. Male or female hormone replacement are not funded by the NHS, which seems perverse when other long-term hormone treatments are.

Concluding remarks

The report appeals for organised and equitable funding streams to be developed nationwide for these younger cancer patients, and also calls for a, preferably, research-based egg and ovarian storage facility to be provided nationally – funded either by the NHS and/or research bodies. It is hoped that increasing professional and patient pressure will lead to improved availability of resources for these patients at this very distressing time. There are few more rewarding achievements for patients, and their oncologists, than the production of new offspring despite a sometimes harrowing treatment course for life-threatening cancer.

Members of the Working Party

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References

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2 National Institute for Clinical Excellence. *Fertility: assessment and treatment for people with fertility problems*. London: NICE, 2004.