Teenagers and Young Adults with Cancer

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Fertility

TYAC best practice statement for health professionals

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FERTILITY BEST PRACTICE STATEMENT

Objectives

Guidance for professionals to assist them to:

- Have an informed discussion with teenage or young adult patients (and their family if appropriate) about the potential effects of planned treatment on future fertility.
- Explain options for fertility preservation.
- Ensure timely referral to an appropriate fertility expert.
- Signpost teenagers and young adults to appropriate ongoing support once treatment has completed.

Aims

For the teenage or young adult patient to be fully informed about the potential for infertility and potential options for fertility preservation.

- **Population**
  Teenagers and young adults (TYA): 13 -24 years.
- **Problem**
  Potential infertility.
- **Intervention**
  Fertility preservation where appropriate/available.
- **Outcome**
  All TYA accessing appropriate information and opportunities for fertility preservation.

Introduction

It is well recognised that treatment with surgery, chemotherapy and radiotherapy may affect a patient's future fertility.

The impact of cancer and treatment on future fertility may be different in male and female patients, and varies depending on tumour type, tumour site and treatment received. (Toumaye H, Dohle GR, Barratt CL. 2014).

Evidence suggests that actual clinical practice regarding fertility discussion at the beginning of treatment varies across the UK and a significant proportion of TYA cancer survivors are unable to recall a discussion about fertility at the time of diagnosis, or are dissatisfied with the content of discussions that did take place. (Yeomanson DJ, Morgan S, Pacey AA. 2013).

Patients diagnosed at the younger end of the TYA population may find it especially difficult to understand the relevance of fertility preservation or struggle to envisage how this may impact on life choices they may want to make many years later.

Best practice requires that TYAs with cancer should be provided with full information regarding the risk to their fertility consequent to their treatment, and there should be a discussion regarding the options (or absence of options) for fertility preservation. This should be delivered in a clear, timely and direct manner by someone familiar with the processes involved. (NICE clinical guideline 156: February 2013).

Prior to discussing fertility with patients, the following should be considered:

- Impact of diagnosis on fertility potential.
- All patients have a documented record of baseline fertility assessment.
- Impact of planned treatment on future fertility.
- Prognosis of the cancer treatment.
- Preservation options.
- Expected outcome of subsequent fertility treatment, including likely 'quality' of stored material (NICE clinical guideline 156: February 2013).

NICE clinical guideline 156: Fertility assessment and treatment for people with fertility problems (February 2013) recommends that:

- There is no lower age limit to consider fertility preservation in post-pubertal cancer patients.
- The eligibility criteria for conventional infertility consideration should not be used to determine suitability for fertility preservation. (Although these issues do apply when using stored material for conception).
- Psychosocial support should be offered for discussions about fertility preservation.

Subsequent sections contain current information regarding fertility preservation techniques potentially available to different groups of patients and may be helpful for healthcare professionals planning to discuss fertility preservation with TYAs.

Gold standard service

All TYA patients who are likely to experience fertility complications as a consequence of their disease or management should have access to an experienced fertility specialist/gynaecologist who can discuss fertility options with patients/families. Referrals should be expedited to avoid delays to cancer treatment. Ideally this expert would be a member of the MDT where all new patients are discussed.

Male patients

Pre-pubertal

There are currently no options for fertility preservation in pre-pubertal males. Patients and families should be offered access to a fertility expert to discuss this, at an appropriate time point. There is research interest in testicular cryopreservation for this patient group, but this technique is unproven and should only be considered as part of a research project, if and when one becomes available. (Toumaye H, Dohle GR, Barratt CL. 2014). Professor Wallace has just established this service in Edinburgh as part of a research study for testicular cryopreservation. (See Appendix I).

Post-pubertal males

Sperm cryopreservation is a relatively straightforward and effective option for post-pubertal males. Storage can be arranged relatively quickly, but may not be possible for patients who are particularly unwell or who require immediate treatment. Although a relatively simple procedure, it is vital that the young patient is made to feel comfortable. Being asked to masturbate in an unfamiliar environment with pressures from family to produce samples can have a negative effect on the young person. Sperm cryopreservation should be offered routinely to post-pubertal males who are preparing for medical treatment for cancer that is likely to make them infertile. (NICE clinical guideline 156: February 2013).

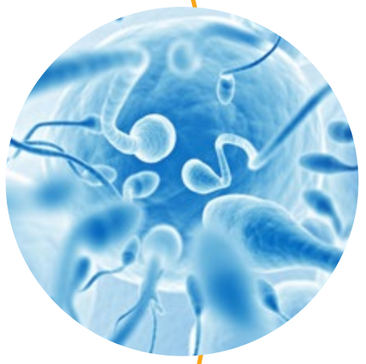
Take care to consider the appropriateness of this conversation, in the context of the disease and clinical status at presentation. All TYA cancer services should identify their local fertility services, ensure they have a clear referral pathway, and a good working relationship with their andrology service. Prior to making a referral to andrology services it is important to explain to the patients (and parents when relevant) what is required of them in providing a sperm sample and to prepare them regarding the nature of the HFEA mandated consent process (General Medical Council 1998), (Human Fertilisation and Embryology Authority 2013).

Individuals must be competent to consent to sperm banking (parents can consent to storage on behalf of the patient if below 16 or deemed not to be Fraser competent. They cannot consent to future use of the gamete). (Larcher V, Hutchinson A. Arch Dis Child. 2010), (Griffith R, Tengnah C. 2012). They will be asked a question about whether the stored sperm should be discarded or continued in storage for future use if they become mentally incapacitated or die. (British Fertility Society 2002). It can be helpful to explain to TYAs that everybody referred to fertility units for sperm storage is routinely asked this question, given that newly diagnosed TYA cancer patients may be extremely distressed if asked to consider the possibility of dying.

In general, initial consent is obtained for sperm storage for 10 years. If continued storage is required thereafter, the consent can be extended with written consent. However, the period of funding for NHS storage may vary with different local funding bodies.

Patients should be referred as soon as possible to allow time for the fertility consultation and freezing of sperm. Ideally three samples will be collected, 24 hours apart, to maximise the chances of successful treatment if this is required at a later date. Even if the sperm quality is poor, it is worthwhile attempting sperm storage as fertility techniques are available where a successful outcome may be achieved using small numbers of sperm. (Crha I, Ventruba P, Zakova J et al 2009). A single collection may be adequate if this is all there is time for, or the patient finds it difficult to produce multiple samples.

Screening bloods for Hepatitis B, C, Hep B core antibody and HIV and in some units Syphilis serology, must be taken prior to referral. It is the responsibility of the referring clinician to ensure that these results are made available when the patient attends for freezing. Different units will use their own policies for storing sperm affected by any of the above. This is to minimise the delay in storage of samples that are stored in screened containers.



Female Patients

Pre-pubertal females

Patients and families should be offered timely access to a fertility expert to discuss fertility preservation options if requested. Ovarian tissue cryopreservation is still considered an experimental technique, but it is the only option currently available for fertility preservation in pre-pubertal girls. (British Fertility Society 2002), (Sonmezer M et al 2004), (NICE clinical guideline 156: February 2013), (Resetkova N, Hayashi M, Kolp LA, Christianson MS. 2013). At the present time this is not a treatment offered within the NHS. However, in selected cases it may be performed only within an approved research protocol. (See Appendix I).

Post-pubertal females

Ovarian stimulation and oocyte or embryo cryopreservation are potential options for female TYA cancer patients undergoing treatment that is likely to impact significantly on fertility. Chemical protection of the ovary with the use of GnRH analogues has been considered for some young women where time does not permit fertility preservation; however there is currently insufficient evidence to guarantee gonadal protection. (NICE clinical guideline 156: February 2013).

Embryo storage is likely to be an option for a minority of patients who are in an established relationship. (Sonmezer M et al 2004). Oocyte preservation may be a more suitable technique for those without a partner willing to undertake fertility preservation. (Anderson RA et al 2008), (Ajala T et al 2010). Both latter techniques take approximately two weeks. Ideally stimulation is commenced at the start of the menstrual cycle, but stimulation can be commenced at other stages in the cycle or the cycle manipulated with hormone therapy to minimise delay in starting chemotherapy. (Sönmezer M, Türkçüoğlu I, Coşkun U, Oktay K. 2011).

Either embryo or oocyte cryopreservation should be considered for TYAs if:

- The patient is well enough to undergo ovarian stimulation and egg collection.

AND

- This will not worsen their condition.

AND

- Enough time is available before the start of their cancer treatment. (British Fertility Society 2002).

Cryopreservation of ovarian tissue is currently undertaken in selected individuals on a research basis only. It involves a laparoscopy and removal of part of the ovary which is frozen. At a later date when the patient has recovered the tissue can be re-transplanted. Further discussion with the fertility clinician can be considered in these cases. Patients need to be Fraser competent to give consent for gonadal tissue preservation or their parents can consent to storage of tissue in the child's best interests. (General Medical Council 1998), (Human Fertilisation and Embryology Act 1998).

Generally initial consent is obtained for storage for 10 years. If continued storage is required thereafter, the consent can be extended with written consent. However the period of funding for NHS storage may vary with different local funding bodies. Use of stored material requires consent from the patient. (General Medical Council 1998).

Communication and pathways - best practice

Fertility is something that would (more than likely) not have been discussed with young people until their cancer diagnosis. It is imperative that health professionals raise the subject of fertility with young people in a timely manner (at the time of diagnosis/treatment). It is helpful to allow them plenty of time to discuss the subject and have questions answered before making a decision about fertility preservation. These discussions are most often overlooked when drug regimens of low gonadal toxicity are administered. Where an individual has a low ovarian reserve, these regimens can reduce fertility. Even for TYA patients who are due to receive less gonadotoxic treatment, it may be preferable to address the topic of fertility at diagnosis rather than in the situation of relapsed disease, when more gonadotoxic therapy might be planned.

Clearly, some young people may be too unwell to consider fertility or it may be in their best interests to start their cancer treatment as soon as possible. However, assumptions and decisions should not be made without the full involvement of the young person and if they want to investigate fertility preservation (and considering the clinical contexts above, this is felt to be appropriate) before they start treatment, this should be facilitated. For those who choose to pursue fertility preservation, it is important for them to be aware that it can be unsuccessful due to their cancer and consequently it is important to provide appropriate support.

Post treatment follow up

Males

Males should be reminded that just because they have had chemotherapy it doesn't mean that they will be infertile. Contraceptive advice should be given at each visit and patients should be given the option to have their sperm levels and quality checked one to two years post treatment.

Females

Previously the return of the menstrual cycle was assumed to indicate a return of fertility. However it is now known that although ovarian function returns, fertility may still be compromised.

This is of particular relevance for young women who have a reduced ovarian reserve and would benefit from fertility preservation pre chemo/radiotherapy. The ovarian reserve can be measured by assessing the Anti Mullerian hormone (AMH). This test is not currently available in all hospitals.

Discussions about fertility, ovarian function, and need for contraception should be regularly revisited throughout treatment and through survivorship, with the young person being aware of their fertility status from the outset and the options that are available to them.

When treatment has resulted in ovarian failure, early referral to the appropriate clinic (oncology fertility service or a clinic with a special interest in premature menopause) should be encouraged.

GVHD post stem cell transplant

Young women who have had a stem cell transplant and develop GVHD should be regularly reviewed by a gynaecologist who is familiar with genital GVHD to identify early genital GVHD and institute appropriate treatment to avoid late complications of vulval vaginal adhesions and stenosis. This service may not be available in all centres.

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Appendix I

Contact details for queries about research fertility preservation options for pre-pubescent girls:
Prof. W. Hamish Wallace, Consultant Paediatric Oncologist
Royal Hospital for Sick Children
17 Millerfield Place, Edinburgh EH9 1LF
hamish.wallace@nhs.net / hamishwallace@me.com

Top Tips

- Have an open and sensitive dialogue in a private area with your TYA, alone if preferred. This is essential and will encourage them to ask questions.
- Establish links with your local centre for reproductive medicine and develop a pathway to facilitate rapid access for consideration of fertility
- Time is of the essence and early referral is recommended to optimise fertility preservation options.
- Remember that although a vital subject to discuss, patients are still young people so sensitivity is paramount.
- Don't be afraid to revisit the subject of fertility with them during treatment.
- Once treatment is complete discuss options for testing fertility status.
- Always bear in mind tumour type and therefore time limits for sperm collection.
- Provide contact details for advice.
- Offer the TYA a health professional of the same gender to talk to if this means they are more comfortable with the discussion.

About TYAC

Teenagers and Young Adults with Cancer is a registered charity and the UK's only membership body open to all professionals involved in the care of teenagers and young adults with cancer. By providing information on best practice and new developments, training and support to our members, we aim to improve the quality of life and likelihood of survival for young people with cancer.

Our vision is that all teenagers and young adults with cancer in the UK receive the best possible treatment and support.

For more information on membership

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