Sperm banking and assisted reproduction treatment for couples following cancer treatment of the male partner

Amir Lass¹, Fidelis Akagbosu and Peter Brinsden

Bourn Hall Clinic, Bourn, Cambridge CB3 7TR, UK

¹To whom correspondence should be addressed at: Serono Pharmaceuticals Ltd., Bedfont Cross, Stanwell Road, Feltham, Middlesex TW14 8NX, UK. E-mail: amir.lass@serono.com

In recent years, the survival of young males suffering from cancer has been improved. Development of new techniques such as IVF and intracytoplasmic sperm injection enables even low quality spermatozoa to be used successfully. It is possible therefore to preserve fertility potential of cancer patients before embarking on adjuvant chemotherapy and radiotherapy. Recognizing the importance of protecting the fertility potential of these young males, we present our recommendations for sperm cryopreservation based on the 11 year experience of Bourn Hall and the British Joint Council for Clinical Oncology consultation report. This paper discusses the options available for patients who recover from cancer to become fathers. In many cases patients are concerned about possible abnormalities and teratogenic risks to their future children who have been conceived naturally or by fertility treatment. The data available in the literature may reassure the medical community that there is no such increased risk. However, due to the relatively small number of children born after such treatment, a long-term follow-up is required. There is an ongoing debate regarding the justification for the programme due to the small number of patients who make use of their banked spermatozoa. The authors believe in the importance of protecting the fertility potential of cancer patients, enabling them to father their genetic children in the future while fighting their illness.

Key words: assisted reproductive techniques/cancer/chemotherapy/semen cryopreservation

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Introduction

Survival rates of young men suffering from various types of cancer have improved dramatically in recent years, due to advanced diagnostic techniques and better treatment modalities. In many cancer subjects sperm quality is already reduced before receiving any treatment (Fossa et al., 1989; Meirow and Schenker, 1995). Further deterioration has been observed due to the damaging effect of chemotoxic agents on spermatogenesis, which may be temporary or permanent (Buchanan et al., 1975; Drasga et al., 1983; Fossa et al., 1985; Johnson et al., 1985; Hansen et al., 1990; Presti et al., 1993; Pont and Albrecht., 1997). The sperm quality following cancer treatment depends on many factors: the initial sperm characteristics, the type of cancer (Lass et al., 1999a), the chemotherapy and/or radiotherapy agents in use, i.e. the dose and number of cycles (Meirow and Schenker, 1995; Pont and Albrecht, 1997). It is impossible to predict who will have normal spermatogenesis and who will become azoospermic. Many of these patients are young men who have not started or completed their families. This factor, combined with the developments in the treatment of male fertility treatment, especially intracytoplasmic injection (ICSI), motivates patients and clinicians to preserve fertility potential of cancer patients before embarking on adjuvant therapy.

Recognizing the importance of fertility potential for young male and female cancer patients, the British Joint Council for Clinical Oncology convened a sub-committee comprising medical and clinical oncologists and fertility specialists that produced a consultation report (Working Party of the Joint Council for Clinical Oncology, 1998). The following recommendations are...
Based on this report and our experience at Bourn Hall Clinic, which has had a successful sperm cryopreservation programme for cancer patients for the last 11 years.

**Recommendation for sperm cryopreservation**

**Awareness of the need to refer cancer patients for sperm cryopreservation**

Men diagnosed with cancer should be referred as soon as possible to a licensed sperm banking unit to give a sample or samples for freezing. We found in a large retrospective study that the median time from diagnosis of cancer to the first semen assessment at Bourn Hall was 3 weeks (range 1 day to 16 weeks). Although the time lag from diagnosis to referral was relatively short in patients with testicular cancer or haematological malignancy, in other malignancies there was a delay of a few weeks to referral for semen cryopreservation (Lass et al., 1998). The causes of the delay were: a lower level of awareness of the need for semen banking by the medical team due to a lack of data about the effectiveness of this option, and a longer investigation period to achieve accurate diagnosis and staging of the primary disease in solid tumours. Although there was no correlation between the time lag and sperm parameters, it is vital to send these patients for semen cryopreservation immediately after diagnosis, to enable them to store sufficient semen samples before starting chemotherapy.

Our impression, after 11 years experience of sperm cryopreservation for these men, is that only a minority of eligible patients is offered sperm cryopreservation. Even men who have previously been treated with chemotherapy or radiotherapy and who have suffered a relapse of their disease should be referred for cryopreservation, because two-thirds of them have spermatozoa suitable for freezing. It should be a top priority to increase the awareness of general practitioners, oncologists, haematologists and patients themselves to the new opportunities opened to them in recent years (Kliesch et al., 1996; Agarwal et al., 1999; Lass et al., 1999b). Regrettably, in the UK, sperm cryopreservation is not widely available as a National Health Service (NHS)-funded service (Working Party of the Joint Council for Clinical Oncology, 1998).

**The sperm cryopreservation programme for cancer patients at Bourn Hall Clinic**

Patients are referred to our unit by Oncology and/or Haematology Specialists in East Anglia, for semen cryopreservation before proceeding with chemotherapy. Their ages range from 14 to 55 years. They are seen by a specially assigned nurse for the programme, and receive an information leaflet. This is followed by consultation with one of the clinic’s medical team, when the logic of semen cryopreservation and the options for future use are discussed. Blood samples are taken for HIV and hepatitis B and C screening. In the UK, spermatozoa can be stored only after patients sign a form [HFEA 96 (6)] which provides consent and instructions for storage and use of the spermatozoa during life and after death. Appropriate, confidential and free-of-charge counselling is an inseparable part of the programme and is always offered to patients. Patients should be made aware of the possibility that up to 15% of men will already be azoospermic at that stage, before they have had any chemotherapy or radiotherapy (Lass et al., 1998).

In our clinic we do not actively follow up the patients after completion of their chemotherapy, therefore we do not have data on their survival or whether they have been able to conceive spontaneously. Patients are advised to give semen samples ~6–12 months post chemotherapy to assess restoration of fertility capacity, but very few have chosen to do so.

**Semen cryopreservation**

Following the detailed consultation, patients obtain sperm samples by masturbation into two dry pots and the pre-freeze semen sample is analysed according to published guidelines (World Health Organization, 1992). Post-thaw analysis is not done routinely because in many cases the sperm concentration is so low that performing this test would jeopardize the amount available for freezing. Any sample with motile spermatozoa, even if it is below the required minimum for standard IVF (in our unit a total of $2 \times 10^6$ motile spermatozoa/ml), should be frozen. Introduction of intracytoplasmic sperm injection (ICSI) technique can bypass even the most severe sperm concentration and motility problems (Working Party of the Joint Council for Clinical Oncology, 1998; Pfifer and Coutifaris, 1999). Cryopreservation is performed on any semen sample containing motile spermatozoa by our routine protocol (Richardson, 1979). Semen is diluted with cryoprotectant and 0.7 ml aliquots are transferred to 1.5 ml screw-top plastic vials to enable future use without the need to thaw the whole sample. Samples are cooled by suspension in vapour phase nitrogen at a rate of approximately $-10^\circ C/min$, for 30 min, and then transferred to liquid nitrogen. Patients are asked to give a sample every 2–3 days until they have had 12 ampoules frozen. However, many of them have had to start chemotherapy treatment immediately and had time to supply only one or two samples. Reassuringly, it has been demonstrated that, in cancer patients, semen after abstinence of 24–48 h has a post-thaw quality similar to semen obtained after longer abstinence period (Agarwal et al., 1995). Therefore, the period from diagnosis to starting chemotherapy treatment can be shortened without jeopardizing the frozen sperm quality.

The quality of frozen spermatozoa following thawing is dependent on its initial quality before freezing (Shekarriz et al., 1995; Padron et al., 1997; Hallak et al., 1999a). The cryopreservation process itself affects cancer patients’ spermatozoa in a manner similar to its effect on donors’ spermatozoa (Hallak et al., 1999b).

**Other considerations before treatment for cancer patients**

**Gonadal shielding**

A special, and sometimes ignored, issue is the protection of testes during abdominal radiotherapy. Hansen et al. analysed semen quality in men who received external-beam irradiation for testicular cancer without gonadal shielding, and found that whilst 51% of patients had low sperm counts before therapy, all of them had low sperm counts 2 years after treatment and 82% of them had persistently low counts at a mean of 8 years after therapy.

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(Hansen et al., 1990). With pelvic irradiation of 5000 cGy, a shield should provide a 99% block. For testicular cancer, standard irradiation doses range from 2500 to 3500 cGy; therefore, shields should allow ≤2% penetration. It is critical that gonadal shielding be used for all men receiving infra-diaphragmatic radiation treatment directed to pelvic lymph nodes in the case of testicular cancer or for any other cancer.

**Hormonal manipulation to protect the testis before cancer treatment**

Glode et al. put forth the theory that the process of spermatogenesis might be slowed or suspended, and therefore protected from the devastating effects of chemotherapy on rapidly dividing tissues, by giving hormones that suppress the hypothalamic–pituitary–gonadal axis (Glode et al., 1981). Researchers have since used a variety of hormonal manipulations in animal models with variable results. In the few studies with human subjects, the results have been largely disappointing (Johnson et al., 1985; Waxman et al., 1987). As experiments are refined, however, it is conceivable that hormonal manipulation may emerge as a testis protective therapy of considerable utility (Turek et al., 1998).

**Testicular tissue banking**

In certain situations, especially in azoospermic males, testicular tissue banking would be appropriate at orchidectomy. One study (Yavetz et al., 1997) reported a pregnancy resulting from frozen–thawed embryos achieved by intracytoplasmic injection of cryopreserved sperm cells extracted from an orchidectomized, seminoma-bearing testis, causing obstructive azoospermia.

**Preservation of testicular tissue before cancer treatment**

A study has described how spermatogenesis could be reinstated in mice sterilized with busulphan by injecting their seminiferous tubules with a suspension of testicular cells derived from an allogeneic donor (Brinster and Zimmerman, 1994). These remarkable results suggested that human testicular cells might be harvested and cryopreserved before the start of chemotherapy and reintroduced into the testis on its completion. A clinical trial testing this hypothesis is underway (Radford et al., 1999).

**Fertility following cancer treatment**

Only 20–50% of cancer patients resume spermatogenesis 2–3 years after completion of treatment (Kreuser et al., 1986; Nijman et al., 1987; Naysmith et al., 1998; Hartmann et al., 1999). A few factors affect the recovery of fertility: the pre-treatment sperm quality, the type of malignancy, with testicular cancer having the worst recovery rates (Naysmith et al., 1998); the treatment modality, i.e. alkylating agents have worst effect, the total therapeutic dose and number of treatment cycles (Meirow and Schenker, 1995; Pont and Albrecht, 1997). Because of the long recovery time for spermatogenesis to resume, patients are advised to give a sperm sample for testing after a year in full remission; thereafter, men who regain their spermatogenesis are encouraged to impregnate their partners naturally. Those who fail to do so have to make the choice of using either the partner’s frozen spermatozoa or donor spermatozoa, and, if they choose the former, the type of fertility treatment they would need (Figure 1).

**Assisted reproduction after cancer treatment using banked spermatozoa**

Where adequate amounts of spermatozoa have been banked and semen quality allows, artificial insemination by husband (AIH) of the female partner using the thawed spermatozoa could be considered. Some centres may then offer gamete intra-Fallopian transfer (GIFT). IVF techniques are generally recommended where the quantity of spermatozoa available is small, suboptimal for intrauterine insemination (IUI) or if female pelvic pathology dictates. The decision to offer ICSI is based on the semen quality pre-freeze and post-thaw. Table I summarizes outcomes of assisted reproduction treatments for cancer patients in published studies which specified using cryobanked spermatozoa.

**AIH**

Sanger et al. reported 115 births after AIH using husband’s or partner’s semen, banked before cancer treatment (Sanger et al., 1992). There were nine miscarriages and seven sets of twins included in the data resulting in 117 pregnancies and 115 livebirths. The reported cumulative pregnancy rates after AIH with cryopreserved spermatozoa ranged from 20 to 45% (Sanger et al., 1992). In general, the number of births reported is an underestimate as semen banking facilities do not receive all data regarding births.

**IVF and ICSI**

Since 1984, few authors have reported individual cases in which healthy babies were born following IVF treatment using frozen spermatozoa to patients diagnosed with cancer (Table I). Levron et al. reported the first pregnancy established after the subzonal

![Figure 1](image-url)
insertion of frozen–thawed spermatozoa obtained from a patient with seminoma and severe oligoasthenozoospermia (Levron et al., 1992). Chen et al. reported a live birth following ICSI using cryopreserved semen from a man with testicular cancer (Chen et al., 1996). Retrospective case series and case reports confirm that even poor quality (either pre-freeze or post-thaw) cryopreserved spermatozoa from cancer patients, irrespective of the length of storage, may provide successful results with techniques such as ICSI (Khalifa et al., 1992; Chen et al., 1996; Hallak et al., 1998; Lass et al., 1998).

Khalifa et al. reported on the outcome of IVF treatment in 10 men with malignant disease who had cryopreserved spermatozoa before initiation of cancer therapy (Khalifa et al., 1992). Fertilization was achieved when the swim-up technique of sperm preparation recovered a mean of $1.8 \pm 0.5 \times 10^6$ spermatozoa/ml and when insemination was performed with at least a calculated motile sperm concentration of $1 \times 10^5$/oocyte. The fertilization rate was 60%. Four patients achieved a pregnancy: two of them delivered a single healthy baby, one delivered triplet healthy babies and one had a preclinical abortion. In two patients (three cycles), no motile spermatozoa were recovered after thawing, and micromanipulation of oocytes for assisted fertilization was performed; although fertilized oocytes were transferred, those couples did not achieve a pregnancy.

Lass et al. reported on 8 years experience of semen cryopreservation in men with malignant disease referred to the unit for semen cryopreservation (Lass et al., 1998). Following chemotherapy, six out of the 191 men who had sufficient suitable spermatozoa for freezing attended the clinic for assisted conception treatment using the frozen semen. Two had successful IUI cycles, each resulting in the delivery of a healthy girl; one couple had conceived in their first IVF attempt, followed by delivery of healthy twins. Two women conceived after ICSI treatment and the sixth woman achieved only a biochemical pregnancy after numerous IVF and frozen embryo replacement cycles.

The fertilizing capacity of cryopreserved spermatozoa from patients with cancer was investigated in 10 patients (Hallak et al., 1998). Of these patients, five had Hodgkin’s disease, two testicular cancer, one leukaemia and two prostate cancer. The length of specimen storage ranged from 14 to 135 months (median 49, interquartile range 24–82). A total of 18 assisted reproduction cycles were performed among 10 couples with an overall pregnancy rate of 50% per couple, with two deliveries, one ongoing pregnancy and two miscarriages. The pregnancy rate per cycle of IVF and ICSI was 36.4% with an implantation rate of 13%.

Audrins et al. reported their experience with semen storage for special purposes at Monash IVF from 1977 to 1997 (Audrins et al., 1999). Eighteen of the 258 men who underwent chemotherapy and/or radiation therapy returned for treatment, and six pregnancies were achieved. Twelve couples attempted a total of 53 cycles of AIH with two conceptions, one resulting in a live birth and the other in a miscarriage. Of the 11 couples who did not conceive by AIH, five attempted IVF procedures and three had live births. Of the three couples who had spermatozoa of insufficient quality for AIH, two conceived using IVF (one couple conceived twice). The couple who conceived twice achieved their

### Table I. Summary of published studies on outcome of gamete intra-Fallopian transfer (GIFT), subzonal insemination (SUZI), IVF and intracytoplasmic sperm injection (ICSI) treatments in cancer patients using pre-therapy cryobanked semen

<table>
<thead>
<tr>
<th>Study (first author)</th>
<th>Diagnosis</th>
<th>Method</th>
<th>No. of patients</th>
<th>No. of pregnancies</th>
<th>No. of deliveries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schill (1984)</td>
<td>Testicular cancer</td>
<td>IVF</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rowland (1985)</td>
<td>Testicular cancer</td>
<td>IVF</td>
<td>2</td>
<td>2</td>
<td>2(^a)</td>
</tr>
<tr>
<td>Naz (1985)</td>
<td>Other cancer</td>
<td>IVF</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Milligan (1989)</td>
<td>Hodgkin’s</td>
<td>IVF</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Davis (1990)</td>
<td>Hodgkin’s</td>
<td>IVF</td>
<td>5</td>
<td>6</td>
<td>7(^b)</td>
</tr>
<tr>
<td>Tournaye (1991)</td>
<td>Seminoma</td>
<td>SUZI</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Levron (1992)</td>
<td>Various cancer</td>
<td>IVF and/or ICSI</td>
<td>10</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Khalifa (1992)</td>
<td>Testicular cancer</td>
<td>ICSI</td>
<td>2</td>
<td>2</td>
<td>4(^a)</td>
</tr>
<tr>
<td>Hakim (1995)</td>
<td>Testicular cancer</td>
<td>ICSI</td>
<td>6</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Hulting (1995)(^c)</td>
<td>Testicular cancer</td>
<td>ICSI</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Chen (1996)</td>
<td>Testicular cancer</td>
<td>ICSI</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Yavetz (1997)</td>
<td>Testicular cancer</td>
<td>ICSI</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rosenlund (1998)(^c)</td>
<td>Testicular cancer</td>
<td>IVF and/or ICSI</td>
<td>15</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Hallak (1998)</td>
<td>Various cancer</td>
<td>IVF and/or ICSI</td>
<td>10</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Agarwal (1999)</td>
<td>Various cancer</td>
<td>IVF and/or ICSI</td>
<td>19</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Audrins (1999)</td>
<td>Various cancer</td>
<td>IVF and/or ICSI</td>
<td>18</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Ramsewak (1999)</td>
<td>Neuroglioma</td>
<td>ICSI</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lass (2000)</td>
<td>Various cancer</td>
<td>IVF and/or ICSI</td>
<td>11</td>
<td>7</td>
<td>6(^b)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>109</strong></td>
<td><strong>74</strong></td>
<td><strong>56</strong></td>
</tr>
</tbody>
</table>

\(^a\)One miscarriage and one twin term pregnancy.

\(^b\)One set of twins.

\(^c\)Fresh spermatozoa used, following chemotherapy for testicular carcinoma.

NS = not specified.
second pregnancy from the transfer of frozen–thawed embryos; the conception resulted in twins. The three couples with co-existing female factors underwent a total of eight cycles of IVF, but no pregnancy resulted.

Rosenlund et al. reported on IVF and ICSI in the treatment of infertility after testicular cancer (TC). Fifteen out of 17 couples evaluated for infertility after TC underwent a total of 21 treatment cycles, resulting in 18 embryo transfers (Rosenlund et al., 1998). Spermatozoa were obtained by transectoral electroejaculation (TE) in 16 cycles, by masturbation in three cycles and by testicular sperm extraction (TESE) in one. Fertilization and cleavage were achieved by IVF in seven cycles and ICSI in 11 cycles; average fertilization rates of 57 and 55% respectively were observed. Twelve clinical pregnancies occurred, of which 11 had been delivered or were ongoing. The ongoing pregnancy rate was 57% per cycle.

Agrawal et al. reported on fertilization and pregnancy outcome of cryopreserved sperm patients with cancer (Agarwal et al., 1999). The 19 men were divided into three groups according to the type of cancers: group I, testicular cancer (n = 5); group II, Hodgkin’s disease (n = 9); and group III, patients with prostate cancer (n = 2), leukaemia (n = 1), metastatic neuroendocrine cancer (n = 1) and thyroid cancer (n = 1). IUI was performed in five patients, IVF in four and ICSI in 10 patients. The fertilization rate, pregnancy rate, and the live birth rate showed no differences between the three cancer groups. They concluded that cryopreserved spermatozoa from cancer patients, irrespective of the type of tumour, are able to fertilize and initiate pregnancy with assisted reproductive techniques.

Special situations

**Post-mortem sperm retrieval and posthumous use of banked spermatozoa**

Post-mortem sperm retrieval with subsequent artificial insemination has been employed for posthumous conception. Ahuja et al. reported pregnancy following ICSI treatment with dead husband’s spermatozoa (Ahuja et al., 1997). A variety of legal questions exist involving the rights and relationships of the deceased, his family and his issue (Kahan et al., 1999).

In the event of a patient dying whose spermatozoa are banked, it is important to realize that subsequent insemination or assisted reproduction treatment in the wife/partner can only take place if the patient provided explicit consent whilst in sound frame of mind prior to death. In the UK, there is no obligation on the Human Fertilisation and Embryology Authority (HFEA)-approved clinic to perform an insemination. However, registered clinics can pass on the samples in appropriate condition to another licensed centre which has agreed to perform such an insemination.

**Retrograde ejaculation and anejaculation following retroperitoneal lymph node dissection for testicular cancers**

Treatment options for men who do not antegrade ejaculate after retroperitoneal lymph node dissection for testis cancer include a trial of sympathomimetic medication, to which ~30% of men respond with some antegrade ejaculation, or rectal probe ejaculation. Hultling et al. treated 10 anejaculatory men after testis cancer treatment with rectal probe ejaculation (Hultling et al., 1995). Successful recovery of spermatozoa was possible in nine out of 10 patients. Six couples used electroejaculation in combination with IVF, and five conceived.

Chung et al. reported the use of ICSI with electroejaculates from anejaculatory men (Chung et al., 1998). The aetiologies of anejaculation included a history of retroperitoneal lymph node dissection for testicular cancers, spinal cord injury and psychological causes. Electroejaculates typically have normal sperm numbers but poor motility, morphology, and functional deficiencies. In all, 13 couples underwent a total of 18 ICSI cycles with clinical pregnancy rate of 55.6% per retrieval and implantation rate of 33.3% similar to the rates obtained in standard IVF for non-male factor infertility or ICSI for male factor infertility.

**Pre-pubertal boys with malignant disease**

Spermatozoa can be obtained by masturbation from about the age of 14 years (Kliesch et al., 1996). The only possible option for younger boys is to donate a testicular biopsy for sperm maturation in vitro at a later stage. This technique, not yet tested clinically, raises many ethical, efficacy and safety dilemmas (Bahadur et al., 2000).

**Monitoring of children born after fertility treatment**

From our experience, patients are mostly concerned with the following dilemmas:

- What are the chances of natural conception following cancer treatment?
- What are the risks for the future children from using frozen spermatozoa obtained while having malignant disease?

A recent survey of 283 survivors of cancer from the Cleveland Clinic Foundation tumour registry (men and women) examined their attitudes, emotions, and choices with regard to having children (Schover et al., 1999). Nineteen per cent had significant anxiety that their cancer treatment could affect negatively their children’s future health, and only 57% received information from their healthcare providers about infertility after cancer. Other reproductive concerns were discussed less often.

Patients with cancer may have chromosomal abnormalities in the malignant cell of origin (Testoni et al., 1996), and an increased frequency of human sperm chromosomal abnormalities after radiotherapy has been reported (Martin et al., 1986). However, reassuringly, a few studies have shown that children born after completion of cancer treatment have no increased risk for chromosomal abnormalities or birth defects before or after treatment (Senturia et al., 1985; Hansen et al., 1991; Nygaard et al., 1991; Chatarjee and Goldstone, 1996; Hartman et al., 1999).

Nicholson and Byrne examined fertility and pregnancy of survivors after treatment for cancer during childhood and adulthood (Nicholson and Byrne, 1993). They summarized their comprehensive literature review with the conclusions that offspring of survivors appear to have no increased risk of childhood cancer or birth defects.

Sankila et al. examined the risk of cancer among 5847 offspring of 14652 survivors of cancer in childhood or adolescence diagnosed since the 1940s and 1950s in Scandinavia for a total
of 86 780 person-years (Sankila et al., 1998). They did not find any evidence of significantly increased risk of non-heritable cancer among these offspring. Thus, survivors of cancer should not be discouraged from having children and can expect a good outcome of pregnancy.

Only scarce data exist on the possible risks for children born after fertility treatment. To the best of our knowledge, only 56 babies have been born so far to couples undergoing assisted reproduction treatment (nine IVF or ICSI) after recovery from cancer. No birth defects or any abnormalities have been described in the literature, but the number is obviously too small for definite conclusion. It is vital therefore to keep records of patients having post-cancer infertility treatment and to monitor the children born as a consequence of these treatments.

Should sperm cryopreservation be offered routinely to cancer patients?

In recent years some authors have raised doubts about the justification and necessity of providing the facilities for banking spermatozoa before chemotherapy because of the relatively small number of men making use of it following completion of treatment and therefore the small number of children born as a result of using cryopreserved spermatozoa (Milligan et al., 1989; Radford et al., 1999).

Indeed, we and others found that only a relatively small minority of patients (<10%) return for fertility treatment (Fossa et al., 1989; Sanger et al., 1992; Audrins et al., 1999; Schover et al., 1999; Lass et al., 2000). During 11 years of running the programme at Bourn Hall Clinic, only 11 (3.6%) of the 306 patients who have banked their spermatozoa before chemotherapy or radiotherapy have returned for assisted reproduction treatment (Table II). These findings are explicable for several reasons: recovery or waiting for possible recovery of gonadal function, short period from original illness, anxiety regarding potential risks for the children and uncertainty about their long-term health and therefore their suitability to be parents. A large group comprised young men who have not yet established family life, and unfortunately, patients who succumbed to their malignant disease. Hallak et al. surveyed 56 patients in their programme who requested to discontinue storing of spermatozoa (out of the total 342 men who banked their spermatozoa) (Hallak et al., 1998). Reasons for disposal of spermatozoa were patient death (n=21); fertility, but no plans for more children (n=23); good sperm quality (n=8); and no plans to have children (n=4). They concluded that most patients decided to discontinue sperm banking because either they regained fertility or had improved semen quality. The authors concluded that sperm banking should be strongly recommended for all patients with malignant diseases who may wish to have children, even if they eventually decide that the specimens are not needed. We support this conclusion and believe that the medical community should not be deterred from offering the sperm-freezing service to patients.

The Cleveland survey revealed that, of those currently childless, 76% wanted children in the future. Moreover, ~80% of the sample viewed themselves positively as actual or potential parents. The great majority of younger cancer survivors see their cancer experience as potentially making them better parents. Feeling healthy enough to be a good parent after cancer was the strongest predictor of emotional well-being. Patients’ knowledge that their fertility potential is secured would help in the emotional battle against the cancer. Many, however, are left with significant anxieties and insufficient information about reproductive issues. The improvement in cancer treatment and life expectancy, combined with greater awareness for the fertility options and careful reassurance of the survivors regarding the safety of their children, will undoubtedly increase the number of patients requesting sperm freezing and using it following recovery.

Sperm cryopreservation should therefore be offered routinely to all cancer patients less than 55 years old (the maximum age for freezing spermatozoa by the HFEA regulation) (Working Party of the Joint Council for Clinical Oncology, 1998), and especially to young men who have not yet completed their family. Local protocols should exist to ensure that health professionals are aware of the value of semen cryostorage in these circumstances, so that they deal with the situation quickly and effectively (Working Party of the Joint Council for Clinical Oncology, 1998). The authors strongly believe that the freezing process and use of the spermatozoa in the future fertility treatment, regardless of the method, should be funded by the State as part of fighting malignancy and its consequences.

New options for preserving male fertility of cancer patients might become available in the future. Radford et al. recently described an unpublished study in which human testicular cells are harvested before chemotherapy and reintroduced into the testes on its completion (Radford et al., 1999). There are no results yet on semen analysis following this procedure. This technique would enable indefinite sperm production, natural conception and would be applicable to pre-pubertal boys.

### Table II: Outcome of assisted conception treatment cycles using frozen spermatozoa for patients with cancer

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hodgkin’s lymphoma</td>
<td>IVF×3</td>
<td>NP</td>
</tr>
<tr>
<td>2</td>
<td>Hodgkin’s lymphoma</td>
<td>FER×4</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Multiple myeloma</td>
<td>IVF×2</td>
<td>NP</td>
</tr>
<tr>
<td>4</td>
<td>Hairy cell leukaemia</td>
<td>IUI</td>
<td>Healthy boy</td>
</tr>
<tr>
<td>5</td>
<td>Gastric cancer</td>
<td>IUI</td>
<td>NP</td>
</tr>
<tr>
<td>6</td>
<td>Non Hodgkin’s lymphoma</td>
<td>IUI</td>
<td>Healthy girl</td>
</tr>
<tr>
<td>7</td>
<td>Hodgkin’s lymphoma</td>
<td>IUI×5</td>
<td>NP</td>
</tr>
<tr>
<td>8</td>
<td>Testicular cancer</td>
<td>IUI</td>
<td>Failed to fertilise</td>
</tr>
<tr>
<td>9</td>
<td>Hodgkin’s lymphoma</td>
<td>ICSI×2</td>
<td>NP</td>
</tr>
<tr>
<td>10</td>
<td>Acute lymphocytic leukaemia</td>
<td>IUI×3</td>
<td>NP</td>
</tr>
<tr>
<td>11</td>
<td>Non-Hodgkin’s lymphoma</td>
<td>IUI</td>
<td>Healthy girl</td>
</tr>
</tbody>
</table>

NP = non-pregnant; FER = frozen embryo replacement; ICSI = intracytoplasmic sperm injection; IUI = intrauterine insemination.
However, until these methods become established, and more importantly, until their safety is ensured without risk of transmitting the cancer back to patients, sperm cryopreservation is strongly advised.

References


Rosenlund, B., Sjöblom, P., Tornblom, M. et al. (1998) In-vitro fertilization...

*Assisted reproduction for male cancer patients*

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