Ontario Network of Experts in Fertility
life through knowledge
McMaster University Department of Obstetrics and Gynecology
3210 Harvester Road,
Burlington, Ontario, L7N 3T1
P 1.877.663.0223 F 905.639.3810
www.onefertility.com

Cancer Treatment: Effects on Sperm Quality and Function

By Mike Neal,_BSc. (Hons), MSc
Scientific Director ONE Fertility

Fertility preservation has become an important aspect of cancer treatment and counseling for patients of reproductive age. More successful therapies have led to an increased awareness of quality of life issues for cancer survivors. The ability to have children after over-coming a diagnosis of cancer is a significant quality of life goal for many patients.

For men, the ability to produce competent sperm is critical in maintaining their reproductive potential. Cancer itself may be correlated with low sperm counts and compromised sperm quality. Impaired spermatogenesis is commonly observed in patients diagnosed with testicular germ cell tumors (TGCT) and lymphomas [1-3]. TGCT is related to testicular dysgenesis syndrome which also results in deficient sperm production and higher incidence of cryptorchidism [4]. Gonadal deficiency associated with lymphoma is thought to be a result of a systemic effect of the disease [5].

Treatment of cancer may add further insult to gonadal function resulting in compromised sperm production, quality, motility and DNA damage caused by chemo- and/or radiation-therapy. However, this negative affect may be reversible in part or fully depending on the requirement for surgery involving the gonads; the drug type and dose; radiation location and dosage; and the patients' pubertal status at the time of treatment. Adult male germinal cells are believed to be more susceptible to damage than pre-pubertal testicular cells suggesting that maturation of the testis at the time of cytotoxic insult may influence the degree of damage. Alkylating agents (ie: mustine, vincristine, procarbazine, cyclofosfamide) cause permanent azoospermia in approximately 90% of patients. More recent treatment regimens using a combination of non-alkylating drugs (ie: adriamycin, bleomycin, vinblastine, decarbazine - ABVD) has been shown to be less detrimental to gonadal function and 90% of patients had a recovery in spermatogenesis [6]. In addition to compromised steroidogenesis and sperm production there is concern surrounding the cytotoxic effect on the sperm after treatment. Even with recovery of spermatogenesis the question of sperm quality comes to the forefront when discussing the ability for male cancer survivors to have their own offspring.

Assessment of sperm DNA integrity has been proposed as a method to determine the impact of cancer and cancer therapy on sperm function. The DNA fragmentation index (DFI) can be determined by using the sperm chromatin structure assay (SCSA) which measures the percentage of damaged sperm [7]. The higher the DFI the less likely the sperm will be able to fertilize an oocyte and result in a successful pregnancy. In a recent study Smit et al., (2010) used DFI to investigate the sperm DNA integrity in cancer patients before and after cytotoxic treatment [8]. They found that the cancer did not negatively affect the sperm DNA integrity in TGCT and Hodgkins Lymphoma (HL) patients. Non Hodgkins Lymphoma (NHL) showed an increased DFI at time of diagnosis compared to their healthy counterparts [8]. Furthermore, the DFI decreased

3210 Harvester Road,
Burlington, Ontario, L7N 3T1
P 1.877.663.0223 F 905.639.3810
www.onefertility.com

significantly after cancer treatment in general. This finding suggests that sperm with abnormal chromatin may be more vulnerable to the cancer treatment, leaving a greater proportion of normal spermatogonia from which spermatogenesis resumes after a recovery period [9]. Moreover, radiation therapy resulted in more DNA damage than chemotherapy treatment alone.

Sperm banking is a well-established and recommended fertility preservation option for men diagnosed with cancer. Successful treatment of infertility due to low sperm counts, low motility and/or quality has been greatly enhanced by the use of intracytoplasmic sperm injection (ICSI) which is a manipulation technique that incorporates the selection of a single sperm under a high-powered microscope and injection directly into the female egg to optimize fertilization. Freezing sperm prior to cancer treatment provides hope for the future and an opportunity for men to have their own biological children even if their sperm function and quality is compromised by cancer treatment. Aside from hereditary genetic syndromes, there is no evidence that cancer or treatment for cancer increases the risk of congenital anomalies in the offspring of cancer survivors.

References:

1 Gandini L et al. Testicular Cancer and Hodkin's disease: evaluation of semen quality. Hum Reprod 2003, 18:796-801.

2 Howell SJ and Shalet SM. Spermatogenesis after cancer treatment: damage and recovery. J Natl Cancer InstMonogr 2005, 34:12-17.

3 vanCasteren et al. Use rate and assisted reproduction technologies outcome of cryopreserved semen from 629 cancer patients.FertilSteril 2008, 90:2245-2250.

4 Skakkebaek NE. Testicular dysgenesis syndrome: and increasingly common developmental disorder with environmental aspects. Hum Reprod 2001, 16:972-978.

5 Rueffer et al. Male gonadal dysfunction in pateints with Hodgkin's disease prior to treatment. Ann Oncol 2001, 1307-1311.

6 Fossa SD and Magelssen H. Fertility and reproduction after chemotherapy of adult cancer patients: malignant lymphoma and testicular cancer. Ann Oncol 2004, 15(4):259-265.

7 Evenson D et al. Utility of the sperm chromatin structure assay as a diagnostic and prognostic tool in the human fertility clinic. Hum Reprod 1999, 14:1039-1049.

8 Smit et al. Sperm DNA integrity in cancer patients before and after cytotoxic treatment. Hum Reprod 2010, 25(8): 1877-1883.

9 Spermon et al. Sperm integrity pre- and post-chemotherapy in men with testicular germ cell cancer. Hum Reprod 2006, 21: 1781-1786.

3210 Harvester Road,
Burlington, Ontario, L7N 3T1
P 1.877.663.0223 F 905.639.3810
www.onefertility.com

Michael Neal is a Co-founding Partner and the Scientific Director of ONE Fertility (www.onefertility.com). He completed his Masters Degree in Biomedical Sciences at the University of Guelph, focusing on the reproductive consequences of chromosome abnormalities. His career in Human IVF started by working in a private clinic in Toronto, and he has since worked as a Laboratory Manager in public and private clinics from 2000.

Michael Neal's experience in clinical Assisted Reproductive Technologies and his keen research interests have gained him an international reputation for innovation and excellence. He has numerous peer-reviewed publications and is a frequent reviewer for many major scientific journals related to reproduction. He is a recipient of the prestigious Laboratory Innovation in Fertility and Embryology (LIFE) Award. Other honours include: Best Basic Science Paper, Best Clinical Paper, Alpha Exchange, and the R.T. Weaver Award, among other acknowledgements. In addition to his clinical responsibilities, Mike has research interests in the following areas: (a) the effect of environmental contaminants on fertility, (b) non-invasive measurements of embryo quality, and (c) fertility preservation for male and female oncology patients.

Mike is a member of the Canadian Fertility and Andrology Society (CFAS); the American Society for Reproductive Medicine (ASRM); International Society for Fertility Preservation (ISFP); European Society of Human Reproduction and Endocrinology (ESHRE). He is a past executive member of the ART Lab SIG and CFAS Board of Directors and is also on the Advisory Board of Fertile Future, a non-profit organization dedicated to helping cancer patients preserve their fertility.