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Freezing semen doubles the chances of fatherhood for men after treatment for Hodgkin lymphoma

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Men with Hodgkin lymphoma who want to become fathers after their cancer treatment have greatly increased chances of doing so if they have frozen and stored semen samples beforehand, according to research published online today (Wednesday) in Europe's leading reproductive medicine journal *Human Reproduction*.

In the first study to investigate the impact on fatherhood of freezing semen prior to cancer treatment, researchers questioned 902 male survivors of Hodgkin lymphoma in five European countries (France, Belgium, The Netherlands, Italy and Switzerland) and found that among the 334 who wanted to have children, the availability of frozen semen doubled their chances of doing so when compared with men who had not frozen their semen.

Dr Marleen van der Kaaij (MD), who carried out the work while she was a PhD student at the University Medical Centre in Groningen (The Netherlands), said: "Our study shows that cryopreservation of semen before cancer treatment has a large impact: one in five children born after Hodgkin lymphoma treatment was born using cryopreserved semen. Among survivors wishing to become a father after treatment, availability of cryopreserved semen doubled the odds of successful fatherhood."

She said the findings emphasise the importance of semen

cryopreservation. "Cryopreservation should always be offered to all male patients about to undergo cancer treatment – even in situations where treatment should start urgently or where first-line treatment is not very toxic to fertility. Clinicians should realise the enormous impact of this cheap and simple procedure."

Until now, little has been known about the proportion of cancer patients who freeze semen before their treatment; there have been a few studies from single fertility centres with limited follow-up of the patients. The current study was based on 3399 male Hodgkin lymphoma patients from 13 European countries who had been included in eight, multi-centre, randomised clinical trials of cancer treatments between 1974 and 2004, run by the European Organisation for Research and Treatment of Cancer (EORTC) and the Groupe d'Étude des Lymphomes de L'Adulte (GELA).

In 2008 the researchers sent questionnaires to 1849 survivors in five of the countries and received 902 replies containing the information they needed. The men ranged in age from 15-69, with a median average age of 31. A total of 363 out of the 902 (40%) men had had their semen frozen before starting cancer treatment. Out of these 363 men, 78 (21%) used it following their treatment.

Among the 334 men who wanted to have children after their treatment, 206 (62%) became fathers without any medical assistance, but 128 (38%) were unable to achieve an unassisted spontaneous conception and needed medical help. Frozen semen was available for 99 (77%) of these 128 men; of these 99 men, 78 used the frozen semen and 48 succeeded in conceiving on or more children. Of the remaining 30 men, 27 failed to conceive any children and three had a child spontaneously without the frozen sperm.

Dr van der Kaaij said: "Twenty-three percent of men unable to conceive

spontaneously did not have cryopreserved semen available and could not become fathers. Whereas, among men who did use cryopreserved semen we found a success rate of 62% and several men were still in the process of fertility treatment at the time of the survey. This underlines the importance of making available information and access to cryopreservation facilities for cancer patients."

Treatments for Hodgkin lymphoma have changed over the period of the study and also depend on how advanced the disease is. Both radiotherapy and chemotherapy can be used, but whereas radiotherapy can be targeted to a particular area, chemotherapy is a systemic treatment affecting the whole body. The standard chemotherapy for the disease may use alkylating agents – drugs that damage the DNA of cells – or non-alkylating agents. Alkylating chemotherapy is used widely for more advanced disease and can cause long-term infertility in over 80% of men. However, chemotherapy regimes that do not use alkylating agents are likely to cause infertility in less than 10% of men, and these regimes are more likely to be used for early stage disease.

The researchers found that men treated with chemotherapy were four times more likely to freeze their semen, and twice as likely if they were receiving a second-line treatment for progression or relapse, which would be more likely to be alkylating therapy. Better educated men were 60% more likely to freeze their semen, and men aged older than 30 were less likely to freeze semen than men younger than 30. Men treated after 1994 were more than ten times more likely to freeze semen than those treated between 1974-1983, and men treated between 1984-1993 were four times more likely than men treated before 1984.

"There are a number of probable reasons why men were more likely to cryopreserve semen after 1994," said Dr van der Kaaij. "These include the prevalence of semen cryopreservation facilities and awareness and knowledge of the possibilities, which have steadily increased since the

1970s; fertility preservation techniques really began to become part of regular medical procedures from the 1990s onwards; doctors have grown to be more comfortable with suggesting semen cryopreservation to patients; knowledge on the potentially devastating effects of cancer treatment on fertility has increased from the mid-1980s onwards; and attitudes amongst doctors have changed from being strictly oriented towards survival to including quality of life and other more patient-centred issues."

She concluded: "This paper is part of a large project on long-term treatment toxicity experienced by Hodgkin lymphoma patients. Further projects will focus on other aspects, such as adverse effects on the heart, secondary malignancies and chronic fatigue. We are also planning to publish data on sexuality and relationships."

More information: "Cryopreservation, semen use and the likelihood of fatherhood in male Hodgkin lymphoma survivors: an EORTC-GELA Lymphoma Group cohort study", by M.A.E. van der Kaaij et al for the European Organisation for Research and Treatment of Cancer Lymphoma Group and the Groupe d'Étude des Lymphomes de L'Adulte. *Human Reproduction* journal. DOI: 10.1093/humrep/det430

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