Study suggests most female childhood cancer survivors have good chance of becoming pregnant

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For women who have survived childhood cancer, the impact of modern chemotherapy regimens on the likelihood of becoming pregnant is generally small, and most have a good chance of conceiving, according to one of the largest studies of its kind published in *The Lancet Oncology*. In contrast, male survivors of childhood cancer are significantly less likely to have children, especially if they are treated with chemotherapy regimens containing high doses of commonly used alkylating drugs and cisplatin.

Now that more than 80% of children with cancer are living into adulthood, whether they can have children is a major concern for them. Growing awareness of the adverse effects of radiotherapy has led to the use of more intensive chemotherapy regimens for the treatment of childhood cancers. Previous research has shown that fertility can be compromised by several types of chemotherapy, mainly alkylating drugs. However, little is known about the dose effects on pregnancy from newer drugs, such as ifosfamide and cisplatin, in survivors of childhood cancer.

Dr Eric Chow from the Fred Hutchinson Cancer Research Center, Seattle, USA and colleagues used data from the Childhood Cancer Survivor Study (CCSS) which tracks people who were diagnosed with the most common types of childhood cancer before the age of 21 and treated at 27 institutions across the USA and Canada between 1970 and

1999, and who had survived at least 5 years after diagnosis.

In this study, they examined the impact of various doses of 14 commonly used chemotherapy drugs on pregnancy and livebirth in 10938 male and female survivors, compared with 3949 siblings. The study specifically focused on survivors treated with chemotherapy and who did not receive any radiotherapy to the pelvis or the brain.

By age 45, 70% of female cancer survivors became pregnant, compared to over 80% of siblings. For male cancer survivors, the figure was 50% compared to 80% for siblings.

In male survivors, the likelihood of fathering a child generally decreased as cumulative exposure to alkylating drugs increased. High cumulative doses of several alkylating drugs (cyclophosphamide, ifosfamide, procarbazine) and cisplatin were linked with a significantly reduced likelihood of pregnancy (table 3). The findings are consistent with previous studies which have suggested that men who have undergone cancer treatment with these drugs have lower sperm count and reduced testicular volume. The authors point out that the ifosfamide dose threshold above which male cancer survivors are significantly less likely to father a child is far lower than the dose judged to be high risk in current guidelines (25000 mg/m^2 vs 60000 mg/m^2).

In female survivors, only busulfan and high doses of lomustine were directly linked with lower likelihood of pregnancy (table 3). Overall, female survivors were still less likely to conceive compared to siblings but the effect was much smaller compared to men. However, in women, the difference was more pronounced for those who delayed pregnancy until they were aged 30 or older, possibly because chemotherapy exposure might accelerate the natural depletion of eggs and hasten menopause.

The authors note that their study relied on self-reported pregnancy and livebirth, and that up to a quarter of pregnancies can be unrecognised by women. Although their findings are consistent with others in the field, their study did not account for other factors such as marital or cohabitation status, the intention to conceive or length of time attempting to conceive. While the total number of survivors in the study is large, the number of patients who were exposed to individual drugs varied significantly. So, while the overall conclusions of the study are consistent with previous research studies, more research is needed to estimate the exact risk of some less commonly used drugs.

According to Dr Chow, "We think these results will be encouraging for most women who were treated with chemotherapy in childhood. However, I think, we, as paediatric oncologists, still need to do a better job discussing fertility and fertility preservation options with patients and families upfront before starting cancer treatment. In particular, all boys diagnosed post-puberty should be encouraged to bank their sperm to maximize their reproductive options in the future. The current options for post-pubertal girls remain more complicated, but include oocyte and embryo cryopreservation."

Commenting on the implications of the study, Professor Richard Anderson from the University of Edinburgh, UK and Dr Hamish Wallace from the Royal Hospital for Sick Children, Edinburgh, UK say that this report will enable more accurate counselling of patients about their individual risks. They write, "Awareness is needed of the risk of loss of fertility in male patients treated with alkylating drugs and cisplatin, and for pretreatment referral to fertility services. Semen cryopreservation is fairly straightforward, although substantial gaps remain in its provision and accessibility. Appropriate technologies need to be developed for prepubertal and peripubertal boys in whom semen cryopreservation is not possible. For girls and young women, the data are generally more positive, but emphasise the need for accurate

identification of the relatively small proportion who are at high risk, to avoid subjecting those at low risk to what might be invasive procedures."

More information: *The Lancet Oncology*, www.thelancet.com/journals/lan … (16)00086-3/abstract

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