# Transcript

## Late complications: Fertility

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| 00:00:07 | |
| | I'm Doctor Yasmin Jayasinghe. I'm a Paediatric and Adolescent Gynaecologist and today I'm going to be talking about fertility in cancer survivors.<br>We know that the vast majority of young cancer survivors survive to adulthood and fertility is a major survivorship consideration. A lot of young people are wondering about the impact of cancer treatment on fertility, the impact on pregnancy and the impact on their offspring. |
| 00:00:32 | Oncology treatment paradigms are changing |
| | Most young people are unsatisfied with the content and quality of fertility discussions that they have at diagnosis, during treatment, and during survivorship and they want clinicians to be more proactive so that they can make informed decisions during this time and instigate coping strategies. |
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| | When we look at the impact of fertility on females, cytotoxic treatment depletes the ovarian follicle pool – not only the active mature follicles, but the ovarian reserve, also known as the non-growing follicles. When active follicles are depleted, this elevates FSH and there's accelerated recruitment of immature follicles compounding the damage. |
| 00:01:22 | Impact on fertility: females |
| | There's a greater impact on mature follicles compared to immature follicles, so the impact on fertility is greater after puberty compared to before puberty in females. |
| 00:01:35 | Impact on fertility: males |
| | In males, young age is not protective because cytotoxic treatment not only depletes spermatozoa, but also the germ cells that maintain sperm production in post pubertal life. |
| 00:01:48 | Risk prognostication not an exact science |
| | We try and prognosticate the impact on fertility, but it's not an exact science. So factors such as age, pubertal development, the kind of treatment and the dose of treatment, actually come into play when we try and estimate the impact on fertility. We know that total body irradiation, high dose pelvic radiation, any conditioning for bone marrow transplant, and high dose alkylating agents have a very high risk of impact on a young person. |
| 00:02:25 | Fertility: Females |
| | In females, cytotoxic treatment can cause temporary ovarian failure in about 6%. This means that they may get ovarian failure within 5 years of treatment, but this is usually reversible. The chance of premature ovarian insufficiency or premature menopause by 40 is about 8%, compared to 1% in peers. And the chance of infertility is about 16%. |

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| 00:02:58 | CCSS: Contemporary treatments without radiotherapy |
| | There are some good studies now from the childhood cancer survivor cohort. These are studies of over 10 thousand cancer survivors, from 27 centres in the US and Canada. And what this has shown is that with contemporary treatment, the chance of a male siring a live birth is 40% less compared to healthy siblings. And in females, the chance of having a live birth is reduced by 20%. |
| 00:03:30 | CCSS: Contemporary treatments without radiotherapy |
| | If you look at the left hand column, under 'Males', you can see that high doses of alkylating agents and platens significantly reduce the risk of a live birth. If you look at the other column under 'Females', you can see that the risk is far reduced for cyclophosphamide. However, still very significant for Busulfan and Lomustine. |
| 00:03:56 | Pregnancy in cancer survivors |
| | When we look at the impact of pregnancy in cancer survivors, chemotherapy doesn't increase the overall risk of miscarriage or stillbirth or foetal malformation.<br>For those that have radiation treatment to the pelvis, the situation is quite different. Radiation not only depletes the oocyte pool, but it does also cause fibrosis of the myometrium of the uterus and also impair endometrial function. This means that the uterus has impaired distensability and small volumes of the uterus can result in miscarriage, pre-term labour, abnormal placentation – that means an increased risk of placenta accreta or percreta – and there have even been case reports of uterine rupture. |
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| | There needs to be careful consideration of pregnancy after pelvic radiation. |
| 00:04:54 | International standards of care |
| | International standards of care now recommend that we discuss the impact of cancer treatment on fertility in all patients prior to actual treatment commencing. Guidelines vary however in terms of recommendations about provision of fertility preservation strategies, particularly in children, because there's a lack of safety and efficacy data. This creates dilemmas for paediatric providers. However, there is a lag time, and that has really resulted in a widening of access of fertility preservation procedures for children.<br>In 2013, we developed a fertility preservation taskforce so that we could establish clear guidelines and pathways for fertility care in children. This involved provision of resources to clinicians and patients, so that informed decisions could be made. It also included development of research protocols so that data could be collected on safety and efficacy.<br>Fertility preservation is offered at this centre, under three levels of governance as:<br>• A novel technology.<br>• It has clinical ethics approval for individualised cases.<br>• And research governance for collection of data.<br>So it's not considered standard practice, and there are very few centres that do offer fertility preservation for paediatric patients. |
| 00:06:28 | Fertility preservation options |
| | When we look at fertility preservation options that are available, we can divide them into established procedures and experimental procedures. So in females, established procedures include:<br>• Oocyte collection; and<br>• Ovum donation.<br>In males, it's sperm collection.<br>Experimental procedures include:<br>• Tissue collection procedures such as ovarian tissue collection; and<br>• Testicular tissue collection. |

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| | These are the only options that are really available for pre-pubertal children. |
| 00:07:03 | Oocyte/Egg Freezing (standard) |
| | When we look at oocyte freezing, we now consider this a standard practice. There have been thousands of babies born worldwide with this technique. Basically, ovarian stimulation is required and mature eggs are collected a couple of weeks later. Ideally 20 mature eggs are collected over one or two cycles. For every 10 eggs, three embryos can be obtained, producing one live birth.<br>There's no increase in foetal abnormality with oocyte collection. However, it does require physical and emotional maturity, and we don't generally recommend oocyte collection prior to 17 years of age because oocyte yield might be quite low.<br>Also, it's important to note that there can be a delay in terms of the procedure and oocyte collection. So it may not always be suitable for cancer patients requiring immediate treatment, but it certainly is an option for young women in long term follow-up who have good ovarian function, but are at risk of premature ovarian insufficiency. |
| 00:08:14 | Cryopreservation of ovarian tissue |
| | Cryopreservation of ovarian tissue is where a laparoscopic procedure is performed and around about a third of the ovarian cortex is collected – sometimes the whole ovary can be collected. This tissue has immature follicles in it. There's no lower age limit at which this procedure can be done. It can be done at very short notice, and the procedure itself is safe. |
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| | In terms of efficacy for children, there have been 2 case reports where the tissue collected in childhood was autografted back into the body, and this actually did result in induction of puberty and menses. So we have proof of concept that the ovarian tissue can be collected, it can be frozen, thawed and put back in the body and still work. |
| 00:09:10 | Cryopreservation of ovarian tissue |
| | There is an unknown risk regarding malignant reseeding with autografting of the tissue, and the rates of malignant reseeding are variable in the literature. But this needs to be taken into consideration, particularly for children and adolescents with blood borne cancers. |
| 00:09:28 | TTCP |
| | With testicular tissue preservation, this is where a small piece of testicular tissue is taken under an anaesthetic and is offered to post pubertal children who can't produce a sperm sample. It's also offered to pre-pubertal children, but it's important to note that pre-pubertal children actually don't have sperm – they've got germ cells in their testes. Animal studies have shown that progeny can be produced, but at this stage, mature sperm has not been produced from germ cells in humans.<br>We know that the procedure is safe to do but the tissue can also harbour malignant cells, and could potentially pose a risk for children with particularly blood borne cancers. |
| 00:10:20 | Optimising fertility care in follow-up |
| | When we see young people in Long term Follow-up Clinic, it's important to understand that they might have a diversity of experiences with respect to their fertility care. Some of them will have had fertility discussions and even fertility preservation procedures, and others might not have. It's really important to have clear and consistent discussions around the impact of cancer treatment on fertility, and to provide written information as well.<br>Young people often have questions about pregnancy and risk to offspring as well. It is possible to monitor reproductive function, and this can be done with monitoring development, but also doing blood tests, including gonadotrophins, and anti-malarian hormone levels. AMH levels are a marker of ovarian reserve. They're generally more reliable from 20 years of age and over, although there have been some studies done in children which show some correlation with ovarian function. |

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| | In long term follow-up, if we know that a young person is at risk of premature ovarian insufficiency and they currently have good ovarian function, it is possible at that point to offer oocyte collection to increase that young person's reproductive choices in the future. |
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| | Where fertility preservation procedures have been done in the past in childhood, it's really important to revisit those discussions, because at the time, it's usually the parents that are making the decision for the young person and it's really important that the young person is aware of all the information, particularly the issues around storage laws. In Victoria, storage can occur for 20 years, and beyond that point, an extension is required to keep the tissue under storage. There may be costs involved, and over 18, responsibility for the tissue comes under the guardianship of the young person, rather than the adult.<br>It's important to discuss where the technology is at, with respect to fertility preservation so that survivors have realistic expectations of what this technology can provide for them. And being aware of background rates of infertility, is also important. |
| 00:12:49 | Much bigger than an attempt to preserve fertility per se |
| | Fertility care in young cancer survivors is much more than fertility preservation per se, because we can't necessarily guarantee a future pregnancy or live birth, particularly with the tissue collection procedures in childhood.<br>It's important to hold space for them, so that young people have the opportunity to explore their identity, their sexuality and what fertility actually means to them.<br>It's important to avoid certain pitfalls as well.<br>No decision regarding fertility preservation is a wrong decision, and we can't make any judgements regarding the choice that was made. We can't make any presumptions on what a young person wants regarding their fertility. It's important to use appropriate language around fertility.<br>The other important consideration is that cancer survivors have higher rates of unwanted pregnancy than their peers, and contraception is an important issue.<br>Discussions around fertility can have a profound effect on wellbeing and acceptance of fertility outcome – whether it's a positive outcome or not. So good quality discussions which allow informed decision-making, are the benchmark of good care. |
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| | Thank you for listening. |
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