

# Breaking down the barriers: a new collaborative model providing fertility care for young cancer patients

A recently developed national transport and cryopreservation service improves equity of access to fertility care for young people across Australia

**L**oss of fertility, which is a well recognised complication of cancer treatment, has a significant impact on quality of life and is ranked as one of the top survivorship concerns.<sup>1</sup> Improvements in survival (> 88% for adolescents and young adults) and expansion of fertility preserving options have stimulated rapid evolution of the fertility preservation landscape, aiming to decrease this devastating impact of cancer therapy.<sup>2</sup> In addition to the gonadotoxic burden of cancer treatment, societal trends of delayed fertility mean that there are many young people who have not yet completed or even commenced trying for a family when diagnosed with a life-threatening illness.

Fertility discussion, and provision of services to preserve gametes or tissue, is no longer seen as a distraction or a luxury but is acknowledged as a mandatory part of cancer management.<sup>3</sup> However, barriers to provision of fertility preservation care remain. These include the lack of education of health care providers about both the long term fertility consequences of cancer treatment and the clinical value of available options. There is also often a lack of clarity about whose role it is to educate patients about these options. Importantly, there can be significant logistic, geographic and economic barriers for patients, especially outside the major centres, such that only 4–50% of young people take up fertility preservation in a timely fashion.<sup>4</sup>

Established strategies to preserve fertility for the future include medical therapies to protect the primordial follicle pool, vitrification of oocytes and embryos, and ovarian tissue cryopreservation for females. Mature sperm freezing is undertaken in post-pubertal males, and testicular tissue cryopreservation, while providing the only opportunity for pre-pubertal boys, is still considered experimental.<sup>3</sup>

## Gonadal tissue cryopreservation

Ovarian tissue cryopreservation is the only option for prepubertal girls and may be the only or best option for women at high risk of infertility from cancer treatment, particularly if there are time constraints or safety concerns with other options. Ovarian tissue cryopreservation is no longer considered experimental by peak bodies,<sup>3</sup> and there have been over 140 births



worldwide following ovarian tissue grafting, including several in young women whose ovarian tissue was cryopreserved as pre-pubertal children.<sup>5</sup>

Testicular tissue cryopreservation provides an experimental option for fertility preservation in pre-pubertal boys at significant risk of azoospermia from gonadotoxic treatments. As boys do not produce mature sperm that can be frozen, a treatment involving testicular biopsy and cryopreservation of spermatogonial stem cells, followed by transplantation into the testis after treatment, is proposed to allow restoration of fertility.<sup>6</sup> Recent publications of in vitro sperm maturation and live birth success using the primate animal model provide optimism, such that the joint international consensus statement of peak fertility bodies in 2015 recommended that testicular tissue cryopreservation should be offered for pre-pubertal boys,<sup>3</sup> despite the currently experimental nature of future use, especially as there are no other options. Testicular biopsy can be safely performed and often coordinated concomitantly with other medically necessary procedures without delaying the start of treatment.<sup>7</sup>

While cryopreservation of eggs, sperm and embryos is a routine part of assisted reproductive laboratory activity, the technique for cryopreservation of ovarian and testicular tissue is biophysically different, and very few centres nationally and internationally have established tissue cryopreservation laboratories with validated, published protocols and clinical success after thawing.<sup>8</sup> Due to distance challenges within Australia and lack of resources to meet the needs of these patients, particularly those who reside in rural and remote areas, ovarian and testicular tissue

Genia Rozen<sup>1,2</sup>

Stephanie Sii<sup>3</sup>

Franca Agresta<sup>2</sup>

Debra Gook<sup>1,2</sup>

Catharyn Stern<sup>1,2</sup>

<sup>1</sup> Royal Women's Hospital, Melbourne, VIC.

<sup>2</sup> Melbourne IVF, Melbourne, VIC.

<sup>3</sup> Warrnambool Base Hospital, Warrnambool, VIC.

genia.rozen@mivf.com.au

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cryopreservation is not accessible to over 70% of people who would benefit from this opportunity.<sup>4</sup>

### Establishment of the National Ovarian and Testicular Transport and Cryopreservation Service

To provide equity of access to fertility care, the Fertility Preservation Service at the Royal Women's Hospital in Melbourne has developed the National Ovarian and Testicular Transport and Cryopreservation Service, allowing collaboration between local units and specialised centres, with professional and patient education as part of the program. There are several successful international models for collaborative care with published protocols and data to support transportation and storage of gonadal tissue or gametes in a specialised centre with expertise, health and safety regulations.<sup>9</sup> The live birth rates with and without overnight transportation are comparable.<sup>9</sup>

The Fertility Preservation Service, a partnership between the Royal Women's Hospital and Melbourne IVF, was established 30 years ago. It is the largest service of its kind in Australia, with clinical expertise in counselling, cryopreservation, testing, storage and transport procedures. It sees about 300 patients per year, managed by a multidisciplinary team of fertility specialists, nurses, research scientists, research managers, laboratory staff, counsellors and administrators. There have been increasing referrals each year, reflecting the increased demand. Eighty percent of these are cancer related, with serious medical conditions and gender dysphoria forming the remainder.

The Fertility Preservation Service has built extremely strong relationships with cancer centres, both in Victoria and nationally, and collaborates closely with other fertility preservation units, including the Fertility and Research Centre in NSW and the Royal Children's Hospital Melbourne. It supports data collection for the Australasian Oncofertility Registry.<sup>10</sup> Based on a recent Fertility Society of Australia survey,<sup>11</sup> we believe that Victoria, possibly because of both the dedicated

fertility preservation centre and the well developed collaborative relationships, has the highest rate of patients referred for fertility consultation.

The service stores gonadal tissue from over 1000 patients. Ovarian tissue grafting has been performed in 40 patients, with five children born and a live birth rate of 20% per embryo transferred. There are also mature eggs and embryos which have been cryopreserved from ovarian tissue stimulation. Testicular tissue has been cryopreserved for 163 patients.

The establishment of a centralised national tissue retrieval and transport program allows gonadal tissue harvesting to take place in a local centre with subsequent transportation to the central laboratory for processing, cryopreservation and storage. Communication with the National Ovarian and Testicular Transport and Cryopreservation Service team occurs via a paging service which is checked daily by a dedicated nurse, with treating clinician and, when appropriate, patient follow-up by teleconference. Subsequently, ovarian tissue grafting may be performed at the Royal Women's Hospital or the tissue can be transported back to the local centres. The service also provides follow-up and psychological support for patients, and educational resources to assist with all aspects of fertility preservation, both for patients and health practitioners.

Fertility preservation is a mandatory part of cancer care; the National Ovarian and Testicular Transport and Cryopreservation Service program will improve equity of access to fertility preservation for young women and men around Australia.

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