The long road of fertility

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Surviving childhood cancer comes at a cost; along with temporary but gruelling side effects, the life-saving treatments children receive may render them infertile as adults.

Enter Dr. Kirk Lo, assistant professor of urology.

“In adolescents and young adults, chemotherapy and radiation can wipe out sperm production permanently in about half of patients — it depends on what kind of cancer and what kind of therapy they receive,” said Lo. “So we advise them to bank sperm if they can and we’re trying to make that option accessible.”

With survival rates for many pediatric cancers approaching 70 to 80 per cent, post-therapy infertility is a problem that could affect many thousands of young men in years to come. So Lo is working with the Pediatric Oncology Group of Ontario to develop guidelines around fertility counselling and sperm banking for young cancer patients. But for boys whose cancer strikes before puberty there are no sperm to store.

“We’ve had quite a few requests to preserve stem cells from the testes of these patients before the chemotherapy in the hopes that if they survive, we can use this to establish sperm production in the future.”

Across the globe, researchers are trying to grow sperm from stem cells. Scientists are so confident the puzzle will be solved that hospitals in some countries have established clinical and research protocols to harvest cells from young cancer patients for later use.

“We would go in and take out tiny pieces of testicular tissue when the patient is having another procedure done under general anesthesia — but it is an invasive procedure nonetheless so people have concerns,” Lo said. “They say: If you do not have a reliable way to grow sperm today, is it ethically justifiable to perform an invasive procedure on these boys, who already have cancer?

“But we ask, Is it ethical not to preserve their fertility?”

In a research project supported by the National Institutes of Health, Lo is grafting human testes cells onto immunedeficient mice and experimenting with ways of encouraging the tissue to grow and mature to the point where it could produce sperm.

“The cells are starting to divide and we’re basically at the stage where we’re trying to determine what kind of factors we need to simulate puberty, what kind of change in environment,” Lo said. “So we’re challenging it with different agents including gonadotropins.

“We can see the germ cells go from gonocytes to becoming spermatogonia and a paper from Japan came out this year saying they’ve seen them start to differentiate into spermatocytes. So we’re competing to see who gets there first.”

These experiments won’t necessarily produce “a final technique,” Lo said, but they may help establish the viability of the concept.

“If we can prove that it is possible to grow sperm outside of humans, then more people will find it acceptable to start banking testicular stem cells from these patients,” he said.

The concept still requires fine tuning, Lo said, but given the sophistication of in vitro fertilization programs, “all we need is a single

sperm" to allow a boy who survives cancer today to become a father in a decade or two.

Lo's work is "groundbreaking and incredibly important," said Professor **Keith Jarvi**, head of the men's fertility program at U of T.

"He is one of the first investigators in the world to mature these testes," Jarvi said. "He's gone from a couple millimeters to almost one centimeter in size, so it's increased multiple-fold."

The potential applications for Lo's research extend beyond preserving fertility.

"It's also a model for chemotherapy, for looking at how to reduce or prevent the toxicity of the chemotherapy," Jarvi said. "He's building a human testes model in an animal that would be able to tell him if there were chemotherapeutic agents for this age group that were less toxic or if there were ways of avoiding the toxicity — for example, by giving them some protective agents at the same time."

Although his focus now is on preserving fertility, Lo hopes his model might eventually provide a way to test more than drugs.

"We can introduce toxins at any stage and see if it affects stem cells, does it affect cell division or cell death," Lo said. "The applications for this are huge because we can use this to find out what can go wrong, we can restore fertility and in the future it could be a way to test the effects of new drugs.

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