



New techniques preserve fertility hope for women

For a man battling cancer, preserving the option to have children later in life is simple: store samples of semen. Even a single ejaculate contains millions of sperm that can later be used to fertilize an egg. A woman facing cancer, on the other hand, has far fewer choices, which depend on her age, how much time she has before treatment must begin and the availability of a partner who can provide sperm. Oocytes, or eggs, are particularly vulnerable to chemotherapy and radiation, leaving many women infertile after being treated for cancer. The most successful option for a woman of child-bearing age is to create embryos through *in vitro* fertilization and freeze them. (Even if the woman's ovaries are removed, her uterus can still carry a transplanted embryo to term.) Doctors have turned to this method for over two decades, with a success rate of up to 40%. "That's a procedure that doesn't need improvement," says Kutluk Oktay, director of reproductive medicine and infertility at New York Medical College. Women who don't have a partner can try to freeze unfertilized eggs. But, unlike hardy embryos, eggs are sensitive to chilling. Hundreds of babies have been born with this technique, but the success rate overall hovers around 3%. "It's a big drop from embryo freezing," says Tommaso Falcone, chair of obstetrics and gynecology at the Cleveland Clinic. "[But] within the next five years, we'll solve a lot of the cryogenic challenges for freezing eggs." Those who do have a partner who can supply sperm to create an embryo, however, might face another challenge: it takes about two weeks to stimulate the ovary to produce enough eggs for this procedure—time a woman with cancer may not have. In such cases, doctors can remove egg follicles from an ovary and bathe them in nutrients to turn them into mature eggs. This method, dubbed *in vitro* maturation, also has a low rate of success and carries a higher risk of miscarriage.

As IVF becomes more common, some concerns remain

A more experimental option is to remove strips of ovarian tissue, freeze them, and transplant them back into the woman after treatment. Although researchers are still trying to figure out how to reconnect the tissues to the blood supply, at least four women have given birth after an ovarian transplant. This last method also holds the greatest promise for children. "You're not going to do embryo freezing with a ten-year-old," notes Oktay. In the pipeline are also several drugs that promise to protect ovaries from the effects of chemotherapy. In one trial, Kate Stern of the Royal Women's Hospital in Melbourne and her colleagues gave 18 women, with an average age of 25, a drug called cetrorelix. The drug blocks gonadotropin-releasing hormone, effectively sending ovaries into a prepubertal state. One year after treatment, 94% of the women were ovulating normally, the researchers reported at a conference in July. However, because it was a proof-of-concept study, the trial did not include a control group. In their mid-20s, notes Oktay, many women do ovulate after chemotherapy, but their egg reserve is diminished, and they go into early menopause. It's too early to say whether this might also happen with the participants in the Australian trial. Stern says her team is set to launch a randomized clinical trial to test cetrorelix further. Other candidate treatments, such as the compound sphingosine-1-phosphate, prevent the eggs from self-destructing in response to radiation, but research on those candidates has for the most part been limited to animal models. Pending further studies on these compounds, experts say the best option for preserving fertility in women is still to freeze embryos or eggs. *Apoorva Mandavilli*,