

# Fertility preservation with cryopreservation of ovarian tissue: from experimental to mainstream

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Although the first successful preservation of fertility from the freezing, thawing and grafting of ovarian tissue was reported eight years ago,(1) the technique has remained experimental and confined to a few specialist centres. Now, with the announcement of a first pregnancy (and subsequent live birth) in Italy following the transplantation of ovarian tissue, there are indications that fertility preservation is moving into the mainstream of reproductive medicine and into a greater number of centres.(2)

"[Fertility preservation](#) is now a key component of the management of young [cancer patients](#)," said Dr Gianluca Gennarelli from Clinica Universitaria Sant'Anna in Turin, presenting details of the Italian pregnancy at the annual meeting of ESHRE (European Society of [Human Reproduction](#) and Embryology). "Though still a challenging procedure, the [cryopreservation](#) of ovarian cortex should still be offered to young women and girls ahead of potentially gonadotoxic cancer treatments with a high risk of ovarian failure," he said.

The Italian case described by Dr Gennarelli was remarkable not just because it is Italy's first successful pregnancy and delivery, but also because - with a gap of seven years - it represents one of the longest time intervals yet between the date of tissue freezing and the date of successful transplantation.(3) "It demonstrates that pregnancy can be obtained by this technique even after several years of cryostorage," said

Dr Gennarelli.

The case involved a 21-year-old patient scheduled for high dose chemotherapy and [bone marrow transplantation](#). Just before treatment, in July 2003, she was referred for fertility preservation, with ovarian cortical tissue collected by laparoscopy. Bilateral biopsies of ovarian cortex were sampled (ie, from both ovaries), frozen by slow freezing and stored in [liquid nitrogen](#). As feared, chemotherapy was followed by ovarian failure.

In March 2010, following the patient's request and investigation for fertility restoration, 32 cortical tissue fragments were thawed and sutured to prepared sites. Two months after the tissue grafting, some ovarian function returned and spontaneous follicular development was observed. Over the following months spontaneous menstrual cycles were repeatedly evident and ovulation was confirmed in at least six cycles. In July 2011, 15 months after the [ovarian tissue](#) transplantation, the patient became spontaneously pregnant, and a healthy baby was delivered in March 2012.

The birth is believed to be the 22nd in the world from this technique, and a new indication that the restoration of fertility by this technique is feasible, rapidly evolving and worthwhile for a growing number of patients. Given the increase in cancer survival, and the likelihood that many successfully treated young women and girls will live to enjoy their "reproductive" years, interest in the technique - from both patients and doctors - is sure to grow, said Dr Gennarelli.

The cryopreservation of ovarian tissue is not the only technique suitable for young women, and there is also growing interest in oocyte cryopreservation (especially with developments in vitrification). However, both embryo and oocyte storage require a cycle of ovarian stimulation and collection, which may not be suitable for women with

hormone-dependent cancers or for those who need immediate [cancer treatment](#). The storage of ovarian tissue - which may be performed at short notice - overcomes both those problems.

Nevertheless, Dr Gennarelli conceded that the number of successful cases of fertility restoration is not great, especially in relation to the number of tissue samples now in storage. A further poster presented at this congress - from some of the leading groups in the field - reported that most patients having autologous transplantation of ovarian tissue did so with the intention of having a child, but the recovery of hormonal function was also very important to them. Most transplanted women did recover their ovarian function.(4)

"We and other groups now believe that ovarian tissue freezing for fertility preservation should not be considered experimental but be recognised as a routine clinical practice to be offered in appropriate cases," said Dr Gennarelli. "Age, for example, is one important consideration."

On the question of time between tissue [biopsy](#), freezing and transplantation, Dr Gennarelli said: "We are not aware, so far, of any time limit for cryopreserved ovarian tissue. The recent report by the group of Jacques Donnez further prolongs that time interval even further."

Despite the wider application of ovarian tissue storage for fertility preservation, the relatively small number of babies born suggests that far fewer women after their cancer treatment are taking up their options for pregnancy. "The reasons are probably many," said Dr Gennarelli, "but the simplest might be that not so many patients have reached the age or the decision to conceive. Nevertheless, the babies born worldwide so far indicate that we're moving in the right direction."

**More information:** 1. Donnez J, Dolmans MM, Demylle D, et al. Livebirth after orthotopic transplantation of cryopreserved ovarian tissue. *Lancet* 2004; 364: 1405-1410

2. Future fertility is of increasing importance to cancer patients. One study of more than 600 women with breast cancer indicated that 73% of them expressed some concern about the possibility of becoming infertile after treatment. As a result of earlier detection, advanced treatments and better survival rates in female cancers, interest in fertility preservation techniques is growing. The main techniques for women are embryo and oocyte cryopreservation (which each require ovarian stimulation and egg collection), ovarian suppression (with drugs) during chemo- and radiotherapy, and ovarian tissue cryopreservation. Many research questions remain, but all techniques require the collaborating involvement of specialists in cancer and reproductive medicine.

3. Until very recently, this live birth in Turin was believed to represent the longest time interval between tissue freezing and transplantation for pregnancy. However, an online report on 14 June from the Belgian group of Jacques Donnez describes a gap of ten years between freezing and pregnancy (Donnez J, Jadoule P, Pirard C, et al. Live birth after transplantation of frozen-thawed ovarian tissue after bilateral oophorectomy for benign disease. *Fertil Steril* 2012; doi:10.1016/j.fertnstert.2012.05.017).

4. Sanchez-Serrano M, Dolmans MM, Greve T, Pellicer A, Donnez J, Yding Andersen C. Ovarian function after ovarian tissue autotransplantation; global results in Belgium, Denmark and Spain. Poster 348, ESHRE annual meeting 2012.

Presented as a poster (P-346)

First pregnancy in Italy after autologous orthotopic ovarian tissue grafting

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