# Advances in fertility preservation for children and adolescents with cancer

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Advances in the diagnosis and treatment of childhood, adolescent and adult cancer have greatly increased the life expectancy of young women with cancer, but have resulted in a growing population of adolescent and adult long-term survivors of childhood malignancies who may experience premature ovarian failure (POF) and infertility as a result of aggressive chemotherapy and radiotherapy treatments (indicated for both cancer and bone marrow transplantation (BMT)).

Ovaries are very sensitive to cytotoxic treatment, especially to radiation and alkylating agents, which are classified as high risk for gonadal dysfunction. The type and dose of chemotherapeutic agent are known to influence the progression to ovarian failure, with alkylating agents increasing the risk of POF by a factor of nine. Cyclophosphamide is the agent most commonly implicated in causing damage to oocytes and granulosa cells in a dose-dependent manner. This follicular destruction generally results in the loss of both endocrine and reproductive functions, depending on the dose and the age of the patient. Indeed, Larsen and colleagues reported a four-fold increased risk of POF in teenagers treated for cancer, rising to 27-fold in women between 21 and 25 years of age.

Several options are currently available to preserve fertility in cancer patients and allow them to conceive when they have overcome their disease: embryo cryopreservation, oocyte cryopreservation and ovarian tissue cryopreservation. The choice of the most suitable strategy depends on different parameters: the type and timing of chemotherapy, the type of cancer, the patient's age and partner status.

The only established method of fertility preservation is embryo cryopreservation, according to the Ethics Committee of the American Society for Reproductive Medicine, but this option requires the patient to be of pubertal age, have a partner or use donor sperm, and be able to undergo a cycle of ovarian stimulation, which is not possible when chemotherapy has to be initiated immediately or when stimulation is contraindicated according to the type of cancer.

Cryopreservation of oocytes can be performed in single women who are able to undergo a stimulation cycle, although the effectiveness of this technique is still low, with pregnancy and delivery rates ranging from 1 to 5% per frozen oocyte.

Cryopreservation of ovarian tissue is the only option available for prepubertal girls, and for women who cannot delay the start of chemotherapy. Ovarian tissue can theoretically be frozen using three different approaches: as fragments of ovarian cortex, as an entire ovary with its vascular pedicle or as isolated follicles. The indications for cryopreservation of ovarian tissue in case of malignant and non-malignant disease are summarised in a recent review [1]. For patients who need immediate chemotherapy, ovarian tissue cryopreservation is the only possible alternative.

The main aim of this strategy is to reimplant ovarian cortical tissue into the pelvic cavity (orthotopic site) or a heterotopic site like the forearm or abdominal wall once treatment is completed and the patient is disease-free.

To date, we have performed 11 reimplantations of cryopreserved ovarian cortex. All of them have recovered their ovarian function.

## Conflict of interest statement

None declared.

## References

1 Donnez J, Martinez-Madrid B, Jadoul P, van Langandoncket A, Demylle D, Dolmans MM. Ovarian tissue cryopreservation: a review. *Hum Reprod Update* 2006;**12**:519–35.