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EDITORIAL

Important steps towards materializing the dream of developing an artificial ovary

The relatively new field of fertility preservation has made many advances since 1994 when Gosden and colleagues demonstrated that sheep ovarian tissue could be removed, cryopreserved, and transplanted later on to restore fertility (Gosden et al., 1994). This approach led to the first human live birth in Belgium after re-implantation of ovarian cortex into a woman previously treated for cancer (Donnez et al., 2004) and now more than 60 births have been reported worldwide using this technique. The main patient group to benefit from these methods is young women with cancer facing gonadotoxic sterilising chemotherapy treatment. Whilst this is potentially a beneficial technology, there are concerns that in some cancer types the cryopreserved tissue may contain malignant cells and therefore the transplantation could result in the re-introduction of cancer to disease-free patients. With these concerns in mind, it has been the goal of scientists working in this field to produce an 'artificial ovary' that contains only healthy immature follicles (and stromal cells) but would be free of other contaminating cell types that may be malignant.

Once again the group from Belgium have been pioneers in this area, and a paper published in this issue of *RBMOnline* describes research led by Dr Christiani Amorim that moves us a step closer to achieving this goal (Paulini et al., 2016). This paper demonstrates that isolated human pre-antral follicles embedded in fibrin and transplanted into nude mice are 100% viable after 7 days transplantation. Fibrin has been previously shown to be a viable material to support mouse primordial follicle transplantation and live young have been produced (Kniazeva et al., 2015). So the Belgian study provides the basis for moving forward to make improvements for development of human follicles.

The quest to find the ideal matrix to reconstitute an ovary has been a slow process, beginning with early reports of embedding isolated mouse pre-antral follicles in collagen gel and transplantation leading to large antral follicles (Telfer et al., 1990), then expanding into the field of bioengineering that has resulted in the development of many materials to support follicle development (Shea et al., 2014). However, finding the ideal matrix to support growth, development and recovery of human ovarian follicles has remained problematic because of the need to control rigidity in a matrix for this cell type. Results from some studies using alginate suggest that this may be the way forward (Yin et al., 2016).

The Belgian study provides a clear demonstration that a fibrin formulation incorporating fibrinogen and thrombin created an environment that supported follicle and oocyte development. Follicle recovery rates were low at around 22%, but viability was high. This is a promising study that identifies a viable matrix to produce an artificial ovary, but more work is required to improve recovery rates, and the testing of the normality of oocytes grown in this way should be a priority. Clearly, there is still a long way to go towards the development of an artificial ovary, but significant progress is imminent.

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Evelyn E. Telfer
E-mail address: Evelyn.Telfer@ed.ac.uk

Bart C.J.M. Fauser
E-mail address: office@rbmonline.com