Fertility preservation: challenges and opportunities

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Subfertility is a major health issue worldwide, and one that is growing because of an increasing number of subfertile couples, various causes of decreased fertility, and poorly understood mechanisms. In *The Lancet*, three Series papers on fertility preservation[1–3] discuss the effects of physiological and pathological factors on human fertility, and collectively show that fertility preservation is a potential strategy to combat this predicament.

Fertility preservation can play a pivotal part in reproductive medicine for three reasons. First, fertility preservation is the only option for patients with cancer hoping to conserve their fertility. Advancements in early diagnoses and new treatments have greatly lowered the death rate of young (aged 20–39 years) patients with cancer. For example, cancer mortality decreased by 1·8% per year in men and 1·4% per year in women in the USA between 2006 and 2010.[4] Evidence suggests that most patients surviving cancer who are younger than 40 years expect their fertility to be maintained, or endocrine function to be restored.[5] Second, fertility preservation is attractive for healthy couples who wish to postpone childbearing. According to the China's 6th National Census in 2010,[6,7] the ratio of Chinese women giving birth at an advanced reproductive age (35–49 years) showed a 10% increase compared with the ratio in 2000. The phenomenon of delayed childbearing is also evident in Australia, New Zealand, the USA, and western Europe,[8] and brings a risk of age-related subfertility. In dealing with this consequence of socioeconomic forces, fertility preservation at a young age could reduce the risk of fertility loss in later life; indeed, donated oocytes from young women showed better outcomes in assisted reproductive technology than did the use of older women's own oocytes.[9] Finally, fertility preservation can do a great service to reproductive medicine by development of new techniques such as pluripotent stem cells, with the hope of restoring lost fertility in various diseases, including reproductive cancers.

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Although fertility preservation shows potential value, barriers exist for technique development and implementation. For patients with cancer, a personalised preservation scheme is needed that takes into account age, marital status, status of illness, classification of the patient's tumour, and genetic considerations. Normally, cryopreservation of gonadal tissue is preferred in patients with terminal cancer or preadolescents, and germ cells and embryo cryopreservation are conventionally used in patients who are at risk of or have cancer early in life.[10] For the population with normal fertility, is it reasonable for such people to request fertility preservation? What is the paramount consideration in decision making—ethics, personal willingness, or medical indications? Fully informed consent is important for such persons because of continuing debates about the risks of cryopreservation and in-vitro culture.

To overcome these difficulties and help with fertility preservation in the clinic, several strategies have been proposed.[1] First, the establishment of uniform clinical guidelines is needed, including indication and contraindication for treatment, provision of informed consent, and duties of ethics committees. As a logical step to achieve this goal, a fertility preservation society should be formed, composed of oncologists, reproductive medicine clinicians, and embryologists, with the responsibility of drafting standard operating procedures, and building up an accessible system of clinical practice approved by the International Standardization Organization.[2] Second, active education networks should be developed, for better communication of the latest advances among professionals, explanation of the fundamentals to

the public, and development of new techniques by collaborative workshops, as discussed by Dominic Stoop and colleagues.[3] Finally, technical advances will need integrated efforts by scientists and clinicians in basic research and medicine. Accordingly, regulations should be drafted and implemented to guarantee effective and efficient assessment and translation of techniques. On the basis of our own experiences, clinical research institutions affiliated with universities are well positioned for this endeavour with their strong capabilities in organisation and integration of research, clinical practice, translational medicine, and other professional activities.

Potential strategies have been proposed for applications of stem cells in reproductive medicine, including isolation and storage of stem cells derived from ovarian tissue or spermatogonia, and establishment and differentiation of pluripotent stem cells, as elaborated by Herman Tournaye and Michel De Vos and their respective colleagues in this issue.[1,2] In 2014, the possible use of stem cells for human artificial gamete production, especially for eggs, is far from a mature clinical technique, and research is needed to establish efficacy and safety.

The clear message from the three Series papers[1–3] is about the importance of prevention of fertility loss. To achieve this vital goal for human health, collective efforts need to be made to educate the public as well as professionals to protect fertility by raising vigilance about risk factors, undertaking early detection, valuing doctors' advice, pursuing early treatment, and considering fertility preservation and fertility restoration where feasible.

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