## Lefter to the Editor

## Open vs. closed vitrification system: which one is safer?

Dear Editor,

This writing is closely focused on the two main oocyte freezing procedures, in terms of which technique should be preferred for safety and neonatal outcomes. Cryobiology, as a science, studies all the manifestations connected to the development of life and its conservation at freezing temperatures. The first notions of cryobiology date back to the early 1950s, when the first studies aimed at developing the knowledge of biology were launched.

Since then, much progress has been made with the development of new techniques for shedding a light on the adaptation process at extreme temperatures. Cryobiology constitutes the connerstone of fertility preservation.

Sperm freezing for artificial fertilization procedures and cryopreservation of embryos, oocytes and gonads were important scientific steps in the development of this science. In addition, social freezing as a mean to uphold the reproductive autonomy of women can lessen the need for controversial practices such as embryos freezing<sup>1</sup>.

Knowledge in the field of biotechnology is constantly evolving, particularly in the field of fertility cryopreservation, even more in light of the most recent achievement: ovarian tissue cryopreservation for patients who undergo fertility preservation procedures, following a diagnosis of genital sphere carcinomas at a young age<sup>2,3</sup>, which entails significant psychological repercussions. Vitrification has been shown to be more effective than slow cooling, as it is a procedure that prevents ice crystals formation within cells, leaving cell domains intact<sup>4,5</sup>.

Since the mid-1980s, cryopreservation and conservation of human embryos resulting from assisted reproductive techniques has been used in order to avoid the simultaneous transfer of multiple embryos without losing this valuable human biological material.

Over the past decade, this approach has helped to guide practice towards single embryo transfer, thus allowing multiple pregnancies to be drastically reduced in many countries.

The clinical success achieved by cryopreserved embryos has stimulated embryologists and cryobiologists to pursue this direction. This has repeatedly reopened the debate on whether it was right for future children to be informed as to their biological origins<sup>6</sup> and other implications relative to beginning-of-life ethics<sup>7,8</sup> that also have to do with contentious issues, such as legal safeguards for gametes and embryos<sup>9</sup>.

The researchers' goal was not only to provide the most valid method for embryo cryopreservation at different stages, but also the development of a cryopreservation method for human oocytes that would be met with wide support<sup>10</sup>. Such an undertaking was driven by the need to preserve fertility in young cancer patients set to undergo gonadotoxic therapies and by the restrictive legislation in some countries, which prohibits the cryopreservation of embryos.

Finally, in recent years, reproductive medicine specialists have understood and agreed on how oocyte cryopreservation could be a key procedure for the successful implementation of egg donation programs.

The institution of oocyte banks with cryopreserved gametes, capable of providing patients, embryologists and doctors with more therapeutic alternatives had long been an almost unrealistic scenario.

Vitrification is the physical phenomenon that occurs when the solidification of a solution does not take place through ice crystallization, but rather through an increase in viscosity lead-

ing to a glass-like state. It is a cryopreservation method widely applied to cells and tissues. More and more women today resort to egg donation programs due to their advanced age. Egg donation has always produced the highest pregnancy rates among all assisted reproduction methods, mostly due to the selection of oocytes from healthy young donors<sup>11,12</sup>. The two oocytes freezing techniques by vitrification have often given results that are comparable to the fresh results. Egg freezing has given young patients with PCOS (polycystic ovary syndrome) the opportunity to retrieve more oocytes to vitrify. Overall, such patients have a tendency to produce more follicles and are more at risk of OHSS (ovarian hyperstimulation syndrome<sup>13</sup>). Scientific findings<sup>14</sup> show how supplementation with inositol contributes to ovulation recovery in patients with ovulation defects. The path of the infertile couple is certainly very delicate and a relevant issues risk which has been underestimated for years when inexperienced operators fail to take a "gender-based approach"<sup>15</sup>.

Eggs not only transmit genetic information for developing embryos, but also convey to them energy, nutrients and a mitochondrial genome. An altered expression of genetic information could be caused by defects in the DNA, protein-histones, cytoskeletal system, DNA repair system and systems that regulate gene expression (transduction, transcription, etc.). We can therefore validate and confirm the application of vitrification as a cryopreservation technique for human oocytes and for the preservation of female fertility<sup>16</sup>. The guidelines of the European Parliament (European Parliament and the Council of the European Union, 2004, 2006) have prompted researchers to search for solutions to keep vitrification in aseptic conditions. Nowadays, indications for cryopreservation of oocytes are certainly increasing. Oocyte Social Freezing and egg donation banks can be used with good frequency, since vitrified oocytes seem to have the same potential in terms of fertilization and implantation compared to fresh oocytes. Our main concern is how to cryopreserve biological material in the safest way. All this has certainly given great momentum to studies centered on human reproduction biotechnology. Furthermore, the introduction of new techniques that use stem cells to improve implantation or induce the generation of gametes is currently being explored and debated. In our view, procedures that use cryopreserved stem cells should be carried out in extremely and rigorously safe regimes, and based on currently available evidence, the closed vitrification system should be the way to go for this type of cells.

## Conflict of Interest

The Authors declare that they have no conflict of interests.

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