Breakthroughs in the human embryology laboratory... what are the real triggers?

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In his article, Gabor Vajta elegantly describes how advances in mammalian embryology slow down for a number of reasons, including a lack of innovative thinking probably due to the limited resources dedicated to “research and development” in this field. The picture he paints of IVF laboratory technologies “crystallized” at 20 years ago is harsh but accurate, especially when compared with other fields such as molecular genetics or mobile phones. In this scenario, the fascinating idea of a geneticist and an embryologist from the early nineties time-travelling into this decade of the new century, with the geneticist lost in the new technology and the embryologist perfectly capable of performing their usual lab routine, neatly gives the idea of how time has stopped in the IVF laboratory (1).

But, particularly in the field of human IVF, some changes have taken place in the last 20 years after the “ICSI revolution” during the early nineties (2, 3), undoubtedly the major breakthrough in this field. And it is very interesting to observe that in some circumstances new technologies or procedures were introduced not to improve the final result or to simplify the laboratory routine, but to overcome difficulties caused by strict legal requirements or for marketing reasons.

A striking example of the role indirectly played by legislative limitations is in the field of oocyte cryopreservation. This technique was only considered a safe procedure – and thus worth being marketed and used as a clinical tool – after a critical mass of information regarding its efficiency and safety had been gathered from the “Italian experience”. In 2012 the practice committee of ASRM published its guidelines for oocyte cryopreservation, stating that it should no longer be considered experimental, replacing with this document the one previously published in 2008, in which they warned against the marketing and clinical use of oocyte and ovarian tissue cryopreservation (4, 5). It is interesting to observe that 30% of the papers in the references were published by Italian groups, and the majority of these articles contain data collected from 2004 to 2009, the period of an abstruse, bizarre and exceedingly strict national IVF law, which was later, in 2009, declared unconstitutional and against human rights by the Italian Constitutional Court.

This law (Law 40/04) was approved by the Italian Parliament in February 2004 to regulate assisted reproduction technology. It infringed upon basic human rights and the proper application of IVF technology because it mandated procedures that were against the best interest of the woman seeking pregnancy. The main point of controversy was the combination of a mandatory limit of three embryos for transfer, and an obligation to implant all embryos produced; cryopreservation of excess embryos was prohibited. Obviously, this decreased the chances for most women of achieving pregnancy, while at the
same increasing the number and complexity of procedures they needed to undergo and exposing some to an unacceptable risk of multiple pregnancy (6). This 2004 law was inspired by the desire to protect every newly produced embryo and deeply influenced by the way of thinking of the Catholic Church. In this scenario, only the cryopreservation of gametes was allowed. This involved the female gamete despite the fact that at that time the majority of scientists and international scientific societies considered oocyte cryopreservation an experimental and unsafe technique (4, 7, 8).

On 8 May 2009, the Italian Constitutional Court declared that Law 40/04 was unconstitutional. The most important theoretical point made by the Court was that it did not provide protection to embryos, since it admitted that some of them may not produce a viable fetus. Embryo protection is therefore limited by the imperative to ensure a concrete possibility to achieve a successful pregnancy (9).

Owing to of this law, in Italy between 2004 and 2009 oocyte cryopreservation was used in addition to conventional IVF techniques as a way to circumvent many of the regulative and ethical issues associated with embryo cryopreservation. This period saw the peak in the production of papers concerning oocyte cryopreservation by Italian groups, both basic science studies and clinical reports (10, 11).

At the end of this period, the critical mass of clinical data obtained mainly from the “Italian experience” and a few other groups (12) together with advances in vitrification technologies in the last 20 years (13, 14) definitively boosted human oocyte cryopreservation, by demonstrating that vitrified oocytes perform as well as their fresh counterparts (15-17). Based on these studies, international scientific societies finally took away the “experimental” label from this technology, which is nowadays used mostly for oocyte donation programmes (http://www.sart.org/).

Other examples of new technologies which have been developed in the last 20 years of IVF in response to the introduction of strict laws or quality assurance programmes are the use of automatic witnessing/tracking systems, and improvements in lab environment sterility conditions and/or certification of aseptic procedures (18, 19).

In tracking systems, time lapse microscopy (TLM) plays a crucial role. And one of the major factors in the massive increase in TLM culture systems in IVF labs in the last five years, must be the advances in computer/wireless and smartphone/tablet technology, which allow patients to see the footage of their growing embryo. So, despite the potential positive effect of TLM for embryo selection (20), it seems that the real trigger for the explosion of this technology in IVF units is much more related to customer service and marketing reasons.

Last but not least, the impressive advances in the field of genetics has determined in these last 20 years the worldwide application of PGD/PGS analysis. This is already routine nowadays in the majority of top-level IVF labs and is destined to optimize IVF treatments (21) towards the potential final goal of 100% implantation rate (22). In this specific future scenario, it is the combination between advances in IVF-related technologies (genetic testing), the desire to improve the final result and customer-driven marketing strategy that will be the real trigger of this breakthrough.

References