

VETERINARY SCIENCE Editorial

"Back to Nature": Is the Only Option for Real Improvements in the Future of Assisted Reproductive Technology?

Navid Dadashpour Davachi*

Department of Laboratory Animal Production, Razi Vaccine and Serum Research Institute, Iran

*Corresponding Author: Dr. Navid Dadashpour Davachi, Department of Laboratory Animal Production, Razi Vaccine and Serum Research Institute, Iran.

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It has been recognized that the oviduct play a critical role in mammalian reproduction. Actually, the oviduct served as the site of zona pellucida (ZP) maturation, fertilization and early embryogenesis [1]. Infertility problems forced scientists to find a solution to overcome this important issue. As a part of the solution, assisted reproductive techniques (ART) have been developed. ART is consisted of several *in vitro* manipulations, such as *in vitro* maturation (IVM), in vitro fertilization (IVF), and *in vitro* culture (IVC). These *in vitro* manipulations do a little to alleviate serious concerns about infertility. Using IVM, IVF, and IVC in the treatment of infertility problems, have led to the neglect of the oviduct as a crucial part of the reproductive system. The negligence of maternal environment which is surrounds gametes/early embryo(s) in current application of ART, would be the probable candidate for the very low efficiency, in terms of quality and quantity, in *in vitro* embryo production (IVEP).

One of the most prominent concerns that are raised by scientists would be a pivotal question about probable health issues in adolescent of the in vitro produced creatures. To address the question, two main hypothesis had been developed (1970s). The first one is called "back to nature" and the second hypothesis is known as "let the embryo choose". "Back to nature" philosophy aimed to mimic the reproductive environment. In accordance with this principle, the formulation of culture media was based on components of oviduct and uterine fluids and their naturally occurring concentrations. These media include synthetic oviductal fluid (SOF) based on sheep oviduct fluid [2]; B2, based on cattle oviduct and uterine fluids [3]; human tubal fluid (HTF), based on human oviduct fluid [4]; and mouse tubal fluid (MTF), based on mouse oviduct fluid [5]. These media have only few shared components with reproductive fluids. In other words, it is revealed that the epithelial cells which covered the reproductive tubules secrete a lot of unknown proteins and growth factors in response to the presence of the gametes/embryos [1,6]. The absence of these key factors during IVM, IVF, and IVC may responsible for the low efficiency of the IVEP and possible problems in adolescent health. Therefore, to overcome these problems several strategies have been developed, such as gametes/embryo coculture with somatic cells obtained from different segments of the reproductive organs. In a study conducted by Dadashpour Davachi., et al. [1] it is demonstrated that epithelial cells obtained from different segments of oviduct can influence differentially on in vitro oocytes ZP hardening, polyspermy, and subsequent IVF efficiency. These new findings would be a great evidence for positive potential of the "back to nature" philosophy. The second mentioned philosophy in IVEP is "let the embryo choose". Actually, it known as single medium philosophy (for more reading refers to [6]). Those who advocate "back to nature" assume that the exact metabolic needs of gametes/embryo(s) are changed dramatically during the first 5-6 days of early embryonic life. Furthermore, they believed that a specialized cross talk exists between gametes/embryo(s) and maternal environment. This cross talk may lead to the secretion of autocrine/paracrine embryotrophic factors from maternal reproductive system or even by gametes/embryo(s) per se.

In summary, these evidences showed that a single medium without any helper cell is not compatible with growing and changing demands of gametes/embryo(s). On the other hand, applying "back to nature" philosophy in clinical protocols is so hard and time consuming. However, due to the insufficient clinical data, there is no way to conclude that one philosophy, either "let the embryo choose" or "Back to nature", is superior to the other. However, it needs more randomized and clinical studies to reveal the truth!

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