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The history of assisted reproductive technologies: from prohibition to recognition

Abstract. *The birth of children after infertility treatment of married couples with the help of assisted reproductive technologies has become a reality after many years of basic research on the physiology of reproductive system, development of oocyte's in vitro fertilization methods and cultivation of embryos at pre-implantation stages. Given the widespread use of assisted reproductive technologies in modern medical practice and the great interest of society to this problem, the aim of the study was to trace the main stages and key events of assisted reproductive technologies in the world and in Ukraine, as well as to highlight the activities of outstanding scientists of domestic and world science who were at the origins of the development of this area. The paper used historical methods to study and interpret the texts of primary sources and present scientific historical events. In addition, the current trends in assisted reproductive technologies are covered based on the results of our own, more than 30 years of experience in the field of reproductive biology and medicine, and the achievements of world scientists. As a result of the work, it has been shown that despite certain ethical*

and social biases, the discovery of individual predecessor scientists became the basis for the efforts of Robert Edwards and Patrick Steptoe to ensure birth of the world's first child, whose conception occurred outside the mother's body. There are also historical facts and unique photos from our own archive, which confirm the fact of the first successful oocyte in vitro fertilization and the birth of a child after the use of assisted reproductive technologies in Ukraine. Over the last 20 years, assisted reproductive technologies have continued to grow, addressing many other issues of reproductive potential preservation and infertility treatment. State of the art methods of assisted reproductive technologies include the development of cryopreservation method of gametes and embryos by vitrification, genetic screening of embryos in order to prevent the hereditary diseases transmission and embryo transfer with chromosomal abnormalities, the birth of a child "from three parents" in severe cases of mutations in the mitochondrial genome, etc.
Keywords: *reproductive cells; embryos; in vitro fertilization; first "test tube" child; demography; infertility treatment*

Introduction.

There is no other field of science as assisted reproductive technologies (ART) that have made such an impressive progress from prohibition to recognition, from investigation to clinical implementation. The rapid development of ART and related methods is determined by the social and scientific environment that contributes to its development.

Scientific knowledge was rapidly accumulated during every historical stage of ART development, and there was a transition from empirical to practical research methods.

The modern scientific world is aware of the widespread introduction of ART methods in clinical practice. Unfortunately, only two scientists are well-known, P. Steptoe (1913–1988) and embryologist R. Edwards (1925–2013), who for the first time in the world managed to successfully fertilize an oocyte outside the mother's body, transfer the embryo into the patient's uterine cavity and obtain pregnancy which resulted in the birth of the world's first "test tube" child – Louise Brown.

The purpose of the study was to trace the main stages and key events of ART in the world and in Ukraine, as well as to highlight the activities and figures of outstanding scientists of domestic and world science who were at the origins of the development of this area, and the current trends in ART.

Research methods.

The methodology of the research is based on the principles of historicism, continuity of ideas and discoveries of historical knowledge, and interpretation the texts of primary sources, present scientific historical events. The work carried out the systematization of scientific data obtained in the scientometric databases Medline, PubMed, Cochrane Database of Systematic Reviews.

Results and discussion.

Delving into the historical aspect, the scientific development of ART has begun after microscope invention by the Dutchman Antoni van Levenhuk (1632–1723) in 1677 who studied human sperm and first saw and described spermatozoa.

Artificial insemination is the first mention of an ART method, which dates back to 1783 when the Italian scientist Lazzaro Spallanzani (1729–1799) received offspring due to the artificial insemination of dog (Ariatti & Mandrioli, 1993). Only seven years later, the Scottish physician John Hunter (1728–1793) used this technology for infertility treatment of married couple. He injected the man's semen into the genital tract of his wife who became pregnant and gave birth to a healthy child (Wagoner, 2017).

We should also mention Walter Heape (1855–1929), zoologist and embryologist, professor of Cambridge University, Great Britain. He studied the reproductive function of mammals and first reported the case of rabbits` birth after embryo transfer from one animal to another (Biggers, 1991). The scientist conducted his experiments at his home in Prestwich. He transferred two fertilized eggs obtained from a female Angora rabbit to the upper end of the fallopian tube of a female Belgian hare. The experimental animal gave birth to four rabbits, two of the Belgian hare breed and two of the Angora breed.

Gregory Goodwin Pincus (1903–1967) was an American scientist who had continued the study of his English colleague. He studied the hormonal effects on the reproductive system of mammals. In 1934, he performed the first fertilization of a rabbit oocyte in vitro. In 1936 he published his discoveries after experiments with parthenogenetic activation of oocytes. The scientist retrieved the oocyte and placed it in a mixture of saline and sex hormone. The fertilized oocyte was then transferred to an unpaired female which soon gave birth. It is believed that this experiment was the beginning of the development of *in vitro* fertilization technology (Cohen et al., 2005).

John Rock (1890–1984) was a prominent Boston gynecologist who worked at Harvard University and made a serious attempt to achieve clinical success in fertilizing human oocytes outside the mother's body (Thompson, 2016). In 1948 he and Miriam Menken (1901–1992) have obtained hundreds of oocytes during operative interventions on the female pelvic organs. Week after week Menken followed the same procedure: obtaining oocytes from the follicles on Tuesday, adding sperm to them on Wednesday, praying on Thursday, and looking at the microscope again the next day. Every Friday, when she looked in the microscope, she saw only one unfertilized cell and a pile of dead spermatozoa. She performed it 138 times, more than six years. And, what an incredible coincidence, she managed to fertilize 138 oocytes *in vitro*. The results of their work were published in the journal *Science*. The vagaries of fate did not allow scientists to continue the experiment. The reproductive aim of that time was not to give birth but directed to prevent it. The main goal of scientists was to develop simple and convenient methods of contraception.

In 1959 Min Chueh Chang (1908–1991), a young Chinese reproductive researcher, received an undeniable evidence of *in vitro* fertilized oocyte (Yanagimachi, 2016). He has published more than 300 scientific articles on this research subject. Mature unfertilized oocytes were obtained from female albino rabbits which were injected with sheep pituitary extract. Spermatozoa used for fertilization were obtained from the uteri of albino females mated with albino males 12 hours earlier. Three to four hours after fertilization in a Carrel flask, the oocytes were transferred to another flask containing 50% heated serum in saline and cultured to reach the 4-cell stage. In total, 36 second day embryos were transferred to 6 surrogate females of black color, 4 of which gave birth to 15 albino rabbits.

One of Min Chueh Chang students shared an impressive story. Carrying out one of the experiments he observed the penetration of spermatozoa into the oocyte. The passing of spermatozoon through the Zona pellucida (ZP) of the mammalian oocyte has never been observed before. After a while, the student brought the teacher a draft of an article describing the experiment. After a careful reading and some remarks, the teacher crossing out his name in the line of authors emphasized the importance and participation of his student.

At the same time experiments on *in vitro* fertilization of human embryos were continuing in a private clinic in America. The attending physician had prepared Doris Del-Zio for embryo transfer. However, Vande Wiele, the Head of hospital, had considered the procedure to be very contradictory and forbade it because, in his view, it did not comply with his ethical and moral principles. He believed that ART technology required the resolution of legal issues and adherence to scientific standards of that time. Vande Wiele argued that the procedure violated federal regulations because it was non-sterile. In addition, the doctor suggested that the child after ART might have developmental disabilities which could later lead to parents lawsuits. The couple did file a lawsuit, Dr. Vande Ville caused severe physical and mental suffering for patients due to canceling the embryo transfer. They sued the clinic for $ 1.5 million.

However, not all clinics had such a biased attitude towards ART. Many scientists continued working. The pregnancy after transfer of *in vitro* cultured embryo was reported in 1973 by Australian scientists. Unfortunately, the pregnancy was terminated at an early stage of embryonic development (Kretzer et al., 1973).

At the same time, English gynecologist P. Steptoe and embryologist R. Edwards (Fig. 1) began a joint research on the *in vitro* fertilization of animal oocytes. However, most scientists were skeptical about the success of the development of human embryos outside the body. The main executor of these works was a nurse and embryologist J. Purdy (Steptoe, 2015).

The experimental developments of these scientists have reached clinical trials. P. Steptoe and R. Edwards tried to help infertile couples to have a child. However, most of their colleagues believed that the use of human sperm and oocytes was unethical and contrary to moral principles. The founders of reproductive medicine were denied of state funding for research. Meanwhile, the problem of infertile marriage in the UK was gaining momentum. Patients hopefully participated in experimental cycles of ART.

Figure 1. Scientists who for the first time performed a successful *in vitro* fertilization of human oocyte: on the left side– obstetrician-gynecologist P. Steptoe (1913 –1988), on the right side – physiologist R.Edwards (1925 – 2013) (Wade, 2010).

In 1976 the number of failed treatment attempts already exceeded 500. In those early days of research, and in such an indifferent or even hostile environment, there were some groups of enthusiasts around the world who shared a strong belief in success despite the difficulties and untruths and the value of this new scientific field.

In 1977 a significant event occurred. After in vitro fertilization of the oocyte, the P. Steptoe`s research group received the first pregnancy, which unfortunately turned out to be ectopic, and on July 25, 1978, the treatment cycle ended with the birth of the world's first “test tube” child, a girl named Louise Joy Brown! (Steptoe & Edwards, 1976).

According to the WHO, more than 4 million children are in the world today who were born after ART. According to current statistics it is 2% of newborns (Faddy, Gosden M & Gosden R, 2018).

In 2010, Dr. R. Edwards was awarded the Nobel Prize in Physiology and Medicine for his contribution to the world's scientific achievements. Gynecologist P. Steptoe was not awarded this prize because he died on March 21, 1988.

However, scientists from Bourn Hall were not alone in their research. Several groups of scientists worked on the same problem.

In June 1980, the world's third child conceived by ART was born in Australia. Earlier, the Melbourne Clinic reported two early biochemical pregnancies, which were confirmed by elevated levels of chorionic gonadotropin, thus demonstrating that embryos fertilized *in vitro* can develop to the blastocyst stage *in vivo* and possibly initiate implantation (Lopata, Johnston, Hoult & Speirs, 1980).

In September 1981, ART pioneers from around the world gathered at a meeting in Bourn Hall, Cambridge. They discussed the efforts of Indian scientists to recognize their leadership in *in vitro* fertilization developing. It became known that experiments have been conducted with primitive tools and a household refrigerator in India in October, 1978, resulting in the birth of a "test tube" child. This piece of news was widely reported by the media in India and abroad. However, the doctors' statement was appealed because most of their research was not published in peer-reviewed journals. Due to the lack of scientific evidence, India's leadership in ART is not recognized by the international scientific community.

The path of ART development in Ukraine was also thorny. In 1974, the Ministry of Health of the USSR granted permission for the development and implementation of ART methods in the clinical practice of medical institutions in Moscow, Kharkiv and Leningrad. Valentyn Ivanovych Hryshchenko, a Ukrainian scientist, prominent obstetrician-gynecologist, cryobiologist, cryomedicist, pedagogue, Academician of the National Academy of Sciences of Ukraine, doctor of medical sciences, professor, became the ideological inspirer and organizer of innovative research in Ukraine. At that time, Valentyn Ivanovych was the Head of Obstetrics and Gynecology Department of Kharkiv State Medical University. From 1976 to 1979, he was one of the advisers of World Health Organization (WHO) on the Special Program of Human Reproduction, and since 1980, a WHO expert. From 1983 to 2011 he was the director of the Institute for Problems of Cryobiology and Cryomedicine of the National Academy of Sciences of Ukraine (IPC&C of the NAS of Ukraine). Due to his enthusiasm and creative energy, the results of research have been successfully implemented in clinical practice.

Several scientists who were together with Academician Valentyn Ivanovych Hryshchenko at the origins of Ukrainian reproductive medicine: head of the laboratory for cryobiology of human reproductive system Ph.D. Fedir Vlasovych Dakhno; Reproductologist, Ph.D, senior researcher Volodymyr Ivanovych Pinyaev and embryologist-cryobiologist, Ph.D., senior researcher Natalia Nesterivna Chub (Fig. 2).

Figure 2. Scientists of IPC&C of the NAS of Ukraine who for the first time in Ukraine carried out an oocyte *in vitro* fertilization (Academician V. I. Hryshchenko – on the right, Ph.D. V. I. Piniaiev – in the middle, Ph.D. N. N. Chub – near the microscope) (Author's photo).

This scientific team successfully fertilized oocyte *in vitro* and saw embryo development for the first time in Ukraine on November 30, 1984. It should be noted that equipment and medical supplies were not produced in the USSR, one could only dream of purchasing abroad. They made all consumables themselves from improvised means. For example, they made chambers for incubation of embryos adapting devices from chemical laboratories. The desiccator was used for embryo culturing instead of a thermostat. Laboratory equipment for research was very scarce, for example, inaccessible special dishes for culturing embryos were replaced by glasses that were bought at a watch factory.

As a result of the joint work of Kharkiv scientists, the first Ukrainian "test-tube" child Katya Kulyova was born on March 19, 1991 (Fig. 3).

Figure 3. Katya Kulyova (the first Ukrainian "test tube" child) and F. V. Dakhno (gynecologist, head of the laboratory for cryobiology of human reproductive system in the IPC&C NAS of Ukraine) (Author's photo).

During the analysis of archival materials and primary records of research it was revealed that there was not only the scientific but also the emotional component of the research, which allowed to understand the importance of this event and to assess the efforts of scientists who tried to achieve this goal (Fig. 4).

30 years have passed since the birth of the first "test tube" child. During this period, we have seen the development of areas related to ART. Successful oocyte *in vitro* fertilization depends on many factors, one of which is the quality of the female and male gametes. It turned out that in case of male infertility, the efficiency of using the *in vitro* fertilization method existing at that time was very low. The main problem was that the spermatozoon could not penetrate the thick ZP shell of oocyte. Thus, a

new method of *in vitro* fertilization has been invented. Embryologists began using methods which increase softening of *ZP* (Kiessling, Loutradis, Mcshane & Jackson, 1988), creating a hole in it with an acidic Tyrode`s solution (Gordon, Grunfeld, Garrisi, Talansky, Richards & Laufer 1988), mechanical perforation of *ZP* (Cohen et al., 1988) or complete removal of ZP. Unfortunately, these methods of fertilization led to polyspermia and increased the level of abnormal embryos.

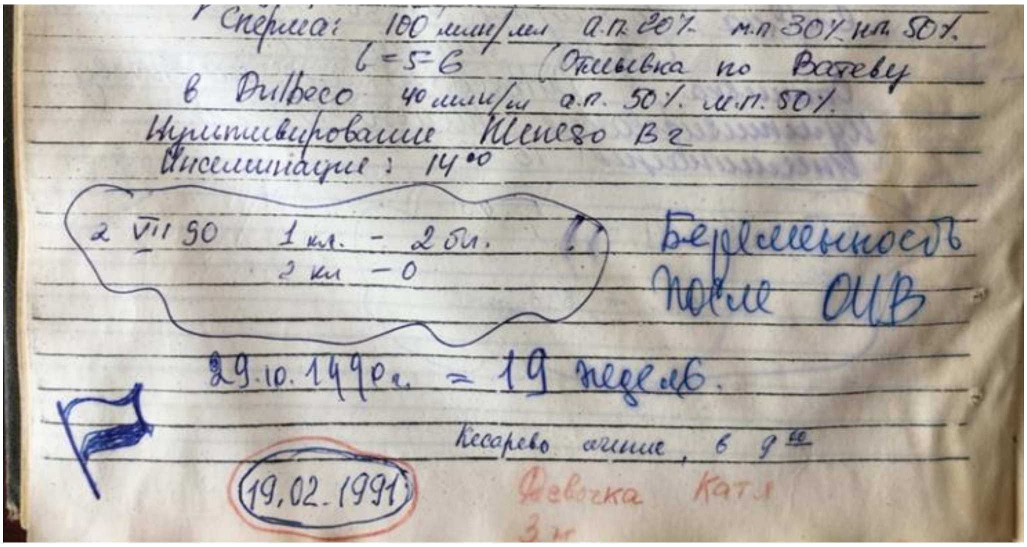

Figure 4. The note in the working journal about the first successful pregnancy in Ukraine after oocyte *in vitro* fertilization and embryo transfer into the patient's uterine cavity (Author's photo).

The method of subzonal insemination (SUZI) also allowed to bypass the *ZP* barrier (Ng et al., 1988). This procedure has been successfully developed for motile spermatozoa, however has been limited in cases of severe male infertility such as asthenozoospermia. In this situation spermatozoon, when introduced into the perivitelline space, does not fuse with the oocyte membrane and fertilization does not occur.

An important milestone in ART was the emergence of technology of intracytoplasmic sperm injection (ICSI) into the ooplasm in 1992 in Brussels (Palermo Neri, Takeuchi & Rosenwaks, 2009). This method is used for infertility treatment of couples with male infertility factor which drastically increases successful ART outcomes.

After the first report about the birth of a child using ICSI, the procedure has been steadily gaining popularity in other European countries, and then spread around the world (Palermo et al., 2017). During the 1990s, the ICSI method proved invaluable while using testicular and epididymal spermatozoa (Schoysman, 1993) in case of absence of spermatozoa in ejaculate, for the fertilization of cryopreserved oocytes (Porcu, Fabbri, Seracchioli, Ciotti, Magrini & Flamigni, 1997), and *in vitro* matured oocytes (Chung et al., 2000). Consequently, advances in reproductive medicine through the capabilities of ICSI have prompted the use of this technique not only according to indications of male infertility (O'Neill, Chow, Rosenwaks & Palermo, 2018).

Another milestone in the ART development is associated with the invention of protocols that allow preserving female and male fertility or excess amount of embryos for subsequent transfer. A breakthrough in this area was creation of oocyte cryopreservation method by vitrification. First childbirth after using this method was reported in 1999 (Kuleshova, Gianaroli, Magli, Ferraretti, Trounson, 1999). More cryobiological approaches for long-term low temperature storage of reproductive cells and preimplantation embryos was invented after that. Most of them are dedicated to increasing survival or improving the capacity for development and further implatation (Petrushko, Yurchuk, Piniaiev & Buderatska, 2019; Yurchuk, Petrushko, Gapon, Piniaiev & Kuleshova, 2021). This includes the introduction of cytogenetic, molecular genetic and molecular cytogenetic studies to determine the aneuploidy of the chromosome set of oocytes and preimplantation embryos (Buderatska, Gontar, Ilyin, Lavrinenko, Petrushko & Yurchuk, 2020). Numerous modifications of ART methods have been made over the years, to improved culture medium for fertilization, optimized cultivation conditions, developed new protocols for cryopreservation of spermatozoa, oocytes and embryos (Petrushko, Yurchuk, & Piniaiev, 2020).

Finally, current research on the creation of an embryo from "three parents" was another unique scientific achievement (Zhang et al., 2017). This incredible invention makes it possible for couples with genetic mitochondrial DNA abnormalities to have offspring.

Of course, many ethical issues stand in the way of developing and improving ART methods. And various associations of the world scientific and public health community regulate their implementation conditions. But looking back at the history of ART development, despite the prohibitions and certain prejudices, the global goal of preserving the humanity will always stimulate the development of technologies and the receipt of new technologies in the field of human and animal reproduction. Professionals in embryology, endocrinology, gynecology, genetics, and anatomy have laid the foundations for future achievements. This is the state of the art of the ART history which we create ourselves in laboratories and clinic cabinets, and which we hope that our descendants will be proud of.

Conclusions.

Being familiar with the scientific achievements in the field of reproductive medicine allows us to conclude that the discovery of ART was not accidental. The basis of today's achievements in the field of reproductive medicine was the long-term work of specialists from different institutions in all fields of science. Brick by brick, experiment by experiment, hundreds of clinical cases, faith and great support from patients have taken the field of infertility treatment to a new level and today more than 5 million children are born who might have never seen this world, but for the scientific achievements of ART.

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Conflicts of interest.
The authors declare no conflict of interest.

References

Ariatti, A., & Mandrioli, P. (1993). Lazzaro spallanzani: A blow against spontaneous generation. *Aerobiologia*, *9*(2-3), 101–107. https://doi.org/10.1007/bf02066251.

Biggers, J. D. (1991). Walter Heape, FRS: A pioneer in reproductive biology. Centenary of his embryo transfer experiments. *Reproduction, 93*(1), 173–186. https://doi.org/10.1530/jrf.0.0930173

Buderatska, N., Gontar, J., Ilyin, I., Lavrinenko, S., Petrushko, M., & Yurchuk, T. (2020). Does human oocyte cryopreservation affect equally on embryo chromosome aneuploidy? *Cryobiology*, *93*, 33–36. https://doi.org/10.1016/j.cryobiol.2020.03.002

Chung, H. M., Hong, S. W., Lim, J. M., Lee, S. H., Cha, W. T., Ko, J. J., . . . Cha, K. Y. (2000). In vitro blastocyst formation of human oocytes obtained from unstimulated and stimulated cycles after vitrification at various maturational stages. *Fertility and Sterility*, *73*(3), 545-551. https://doi.org/10.1016/s0015-0282(99)00546-4

Cohen, J., Malter, H., Fehilly, C., Wright, G., Elsner, C., Kort, H., & Massey, J. (1988). Implantation Of Embryos After Partial Opening Of Oocyte Zona Pellucida To Facilitate Sperm Penetration. *The Lancet*, *332*(8603), 162. https://doi.org/10.1016/s0140-6736(88)90710-6

Cohen, J., Trounson, A., Dawson, K., Jones, H., Hazekamp, J., Nygren, K., & Hamberger, L. (2005). The early days of IVF outside the UK. *Human Reproduction Update, 11*(5), 439-460. https://doi.org/10.1093/humupd/dmi016

Faddy, M. J., Gosden, M. D., & Gosden, R. G. (2018). A demographic projection of the contribution of assisted reproductive technologies to world population growth. *Reproductive BioMedicine Online*, *36*(4), 455–458. https://doi.org/10.1016/j.rbmo.2018.01.006

Gordon, J. W., Grunfeld, L., Garrisi, G. J., Talansky, B. E., Richards, C., & Laufer, N. (1988). Fertilization of human oocytes by sperm from infertile males after zona pellucida drilling. *Fertility and Sterility*, *50*(1), 68–73. https://doi.org/10.1016/s0015-0282(16)60010-9

Kiessling, A. A., Loutradis, D., Mcshane, P. M., & Jackson, K. V. (1988). Fertilization in Trypsin? Treated Oocytes. *Annals of the New York Academy of Sciences, 541*(1 In Vitro Fert), 614–620. https://doi.org/10.1111/j.1749-6632.1988.tb22298.x

Kretzer, D. D., Dennis, P., Hudson, B., Leeton, J., Lopata, A., Outch, K., . . . Wood, C. (1973). Transfer of a Human Zygote. *The Lancet, 302*(7831), 728–729. https://doi.org/10.1016/s0140-6736(73)92553-1

Kuleshova, L., Gianaroli, L., Magli, C., Ferraretti, A., & Trounson, A. (1999). Birth following vitrification of a small number of human oocytes: case report. *Human reproduction (Oxford, England)*, *14*(12), 3077–3079. https://doi.org/10.1093/humrep/14.12.3077

Lopata, A., Johnston, I. W., Hoult, I. J., & Speirs, A. I. (1980). Pregnancy following intrauterine implantation of an embryo obtained by in vitro fertilization of a preovulatory egg. *Fertility and Sterility, 33*(2), 117–120. https://doi.org/10.1016/s0015-0282(16)44529-2

Ng, S., Bongso, A., Ratnam, S., Sathananthan, H., Chan, C., Wong, P., . . . Goh, V. (1988). Pregnancy after transfer of sperm under zona. *The Lancet, 332*(8614), 790. https://doi.org/10.1016/s0140-6736(88)92433-6

O'Neill, C. L., Chow, S., Rosenwaks, Z., & Palermo, G. D. (2018). Development of ICSI. *Reproduction, 156*(1). https://doi.org/10.1530/rep-18-0011

Palermo, G. D., O'Neill, C. L., Chow, S., Cheung, S., Parrella, A., Pereira, N., & Rosenwaks, Z. (2017). Intracytoplasmic sperm injection: State of the art in humans. *Reproduction*, *154*(6). https://doi.org/10.1530/rep-17-0374

Palermo, G., Neri, Q., Takeuchi, T., & Rosenwaks, Z. (2009). ICSI: Where we have been and where we are going. *Seminars in Reproductive Medicine, 27*(02), 191–201. https://doi.org/10.1055/s-0029-1202309

Petrushko, M., Yurchuk, T., Piniaiev, V., & Buderatska, N. (2019). Cryopreservation of incomplete compacted morulae and preliminary biopsy of excluded fragments. *Zygote, 27*(6), 386–391. https://doi.org/10.1017/s0967199419000455

Petrushko, M., Yurchuk, T., & Piniaiev, V. (2020). Oolemma invagination dergree during ICSI as a prognostic criterion for cryopreserved oocyte fertilization. *Cryobiology, 97,* 296. https://doi.org/10.1016/j.cryobiol.2020.10.179

Porcu, E., Fabbri, R., Seracchioli, R., Ciotti, P. M., Magrini, O., & Flamigni, C. (1997). Birth of a healthy female after intracytoplasmic sperm injection of cryopreserved human oocytes. *Fertility and Sterility, 68*(4), 724–726. https://doi.org/10.1016/s0015-0282(97)00268-9

Schoysman, R. (1993). Pregnancy after fertilisation with human testicular spermatozoa. *The Lancet, 342*(8881), 1237. doi:10.1016/0140-6736(93)92217-h

Steptoe, A. (2015). Biology: Changing the world – a tribute to Patrick Steptoe, Robert Edwards and Jean Purdy. *Human Fertility, 18*(4), 232–233. https://doi.org/10.3109/14647273.2015.1077657

Steptoe, P., & Edwards, R. (1976). Reimplantation of a human embryo with subsequent tubal pregnancy. *The Lancet, 307*(7965), 880–882. https://doi.org/10.1016/s0140-6736(76)92096-1

Thompson, C. (2016). IVF global histories, USA: Between Rock and a marketplace. *Reproductive Biomedicine & Society Online, 2*, 128–135. https://doi.org/10.1016/j.rbms.2016.09.003

Wade, N. (2010, October 4). Pioneer of in vitro fertilization wins Nobel Prize. *The New York Times*. Retrieved from https://archive.nytimes.com/www.nytimes.com/2010/10/05/health/research/05nobel.html

Wagoner, N. (2017). John Hunter (1728–1793). Retrieved from http://embryo.asu.edu/handle/10776/11421

Yanagimachi, R. (2016). M. C. Chang: A pioneer of mammalian in vitro fertilization. *Molecular Reproduction and Development, 83*(10), 846–849. https://doi.org/10.1002/mrd.22749

Yurchuk, T., Petrushko, M., Gapon, A., Piniaiev, V., & Kuleshova, L. (2021). The impact of cryopreservation on the morphology of spermatozoa in men with oligoasthenoteratozoospermia. *Cryobiology, 100*, 117–124. https://doi.org/10.1016/j.cryobiol.2021.02.009

Zhang, J., Liu, H., Luo, S., Lu, Z., Chávez-Badiola, A., Liu, Z., . . . Huang, T. (2017). Live birth derived from oocyte spindle transfer to prevent mitochondrial disease. *Reproductive BioMedicine Online*, *34*(4), 361–368. https://doi.org/10.1016/j.rbmo.2017.01.013

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Історія допоможних репродуктивних технологій: від заборони до визнання

Анотація. *Народження дітей після лікування безпліддя сімейних пар за допомогою допоміжних репродуктивних технологій стало реальністю після багатьох років фундаментальних досліджень щодо фізіології репродуктивної системи, розробки методів запліднення in vitro ооцитів та культивування ембріонів передімплантаційних стадій розвитку. Враховуючи широке застосування допоміжних репродуктивних технологій у сучасній медичній* *практиці та великий інтерес суспільства до цієї проблеми метою дослідження було прослідкувати основні етапи та ключові події становлення допоміжних репродуктивних технологій в світі та в Україні, а також висвітлити діяльність видатних вчених вітчизняної та світової науки, які стояли у витоків розвитку цього напряму. В роботі використовувались історичні методи для вивчення та інтерпретації текстів першоджерел та представлення наукових історичних подій. Крім того, на основі результатів власного, більш ніж 30-ти річного досвіду роботи у сфері репродуктивної біології і медицини та досягнень вчених світової науки, висвітлено сучасні напрямки розвитку допоміжних репродуктивних технологій. В результаті роботи показано, що, не дивлячись на певні етичні та соціальні упередження, відкриття окремих вчених-попередників стали підґрунтя для того, щоб зусиллями Роберта Едвардса та Патрика Стептоу народилася перша в світі дитина, зачаття якої відбулося поза організмом матері. Також представлено історичні факти та унікальні фотографії з власного архіву, які підтверджують факт першого успішного запліднення ооцита in vitro та народження дитини після застосування допоміжних репродуктивних технологій в Україні. Останні 20 років допоміжних репродуктивних технологій продовжують невпинно розвиватися, вирішуючи багато інших проблем збереження репродуктивного потенціалу та лікування безпліддя. Серед сучасних методів допоміжних репродуктивних технологій можна виділити розробку способу кріоконсервування гамет та ембріонів шляхом вітрифікації, проведення генетичного скринінгу ембріонів з метою запобігання передачі спадкових хвороб, та переносу ембріонів з хромосомними аномаліями, народження дитини "від трьох батьків" при тяжких випадках мутацій мітохондріального геному та багато іншого.*

Ключові слова: *репродуктивні клітини; ембріони; запліднення in vitro; перша дитина "з пробірки"; демографія; лікування безпліддя*

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История вспомогательных репродуктивных технологий: от запрета к признанию

Аннотация. *Рождения детей после лечения бесплодия семейных пар с помощью вспомогательных репродуктивных технологий стало реальностью после многих лет фундаментальных исследований физиологии репродуктивной системы, разработки методов оплодотворения in vitro ооцитов и культивирование эмбрионов доимплантационных стадий развития. Учитывая широкое применение вспомогательных репродуктивных технологий в современной медицинской практике и большой интерес общества к этой проблеме целью исследования было проследить основные этапы и ключевые события становления вспомогательных репродуктивных технологий в мире и в Украине, а также осветить деятельность выдающихся ученых отечественной и мировой науки, которые стояли у истоков развития этого направления. В работе использовали исторические методы для изучения и интерпретации текстов первоисточников и представления научных исторических событий. Кроме того, на основе результатов собственного, более чем 30-летнего опыта работы в сфере репродуктивной биологии и медицины и достижений ученых мировой науки, освещены современные направления развития вспомогательных репродуктивных технологий. В результате работы показано, что, несмотря на определенные этические и социальные предубеждения, открытие отдельных ученых – предшественников создали фундамент того, что усилиями Роберта Эдвардса и Патрика Стептоу родился первый в мире ребенок, зачатие которого произошло вне организма матери. Также представлены исторические факты и уникальные фотографии из собственного архива, подтверждающие факт первого успешного оплодотворения ооцита in vitro и рождения ребенка после применения вспомогательных репродуктивных технологий в Украине. Последние 20 лет вспомогательных репродуктивных технологий продолжают неустанно развиваться, решая многие проблемы сохранения репродуктивного потенциала и лечения бесплодия. Среди современных методов вспомогательных репродуктивных технологий можно выделить разработку способа криоконсервирование гамет и эмбрионов путем витрификации, проведение генетического скрининга эмбрионов с целью предотвращения передачи наследственных болезней, и переноса эмбрионов с хромосомными аномалиями, рождение ребенка “от трех родителей” при тяжелых случаях мутаций митохондриального генома и многое другое.*

Ключевые слова: *репродуктивные клетки; эмбрионы; оплодотворение in vitro; первый ребенок “из пробирки”; демография; лечение бесплодия*

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