

Nobel Prize for the Development of *in vitro* Fertilization

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Introduction

In memories of Sir Alfred Nobel, the Nobel Prize has been awarded since 1901 to scientists, who have made the most important discoveries for the benefit of mankind which consists of a medal, personal diploma, and a cash award. The Royal Swedish Academy of Sciences has awarded the year 2010 Nobel Prizes in Physiology or Medicine to Robert G. Edwards for "the development of human *in vitro* fertilization (IVF) therapy".

Sir Robert G. Edwards was born in 1925 in Manchester, England. After military service in the Second World War, he studied biology at the University of Wales in Bangor and at Edinburgh University in Scotland, where he received his PhD in 1955 with a Thesis on embryonal development in mice. He became a staff scientist at the National Institute for Medical Research in London in 1958 and initiated his research on the human fertilization process. From 1963, Edwards worked in Cambridge, first at its university and later at Bourn Hall Clinic, the world's first IVF centre, which he founded together with Patrick Steptoe¹. Edwards was its research director for many years and he was also the editor of several leading scientific journals in the area of fertilization. Robert Edwards is currently professor emeritus at the University of Cambridge.

Insights into Infertility and In Vitro Fertilization

Infertility is an inability of a couple to become pregnant (regardless of cause) after 1 year of unprotected sexual intercourse without using any of the birth control methods. Infertility affects about 6.1 million population in the United States². It is a widespread condition affecting more than 10% of all couples worldwide. It is regarded as psychologically stressful by most individuals and can lead to depression, social isolation and a lower quality of life. Medicine had limited opportunities to help these individuals in the past. Today, the situation is entirely different. IVF is an established therapy when sperm and egg cannot meet inside the body. New and advanced technologies to help a

woman become pregnant include IVF, intra-cytoplasmic sperm injection (ICSI), and other similar procedures.

In the early 1950s, researchers started discussion regarding the possible environmental conditions that would otherwise favor human oocytes to be fertilized *in vitro*. In early 1950s, Sir Robert G. Edwards had the vision that IVF could be useful as a treatment for infertility. For the first time he thought and demonstrated that human oocytes can be matured under *in vitro* conditions and it can be fertilized under similar conditions. He worked systematically to realize his goal, discovered important principles for human fertilization, and succeeded in accomplishing fertilization of human egg cells in test tubes (or more precisely, cell culture dishes)³⁻⁵. His efforts were finally crowned by success on 25 July, 1978, when the world's first test tube baby i.e. Louise Joy Brown was born. During the following years, Edwards and his co-workers refined IVF technology and shared it with colleagues around the world. Approximately four million individuals have so far been born following IVF. Many of them are now adult and some have already become parents. A new field of medicine has emerged, with Robert Edwards leading the process all the way from the fundamental discoveries to the current, successful IVF therapy. His contributions represent a milestone in the development of modern medicine⁶.

IVF was used successfully for the first time in the United States in 1981. This offers infertile couples a chance to have a child who is biologically related to them. With IVF, a method of assisted reproduction, a man's sperm and the woman's egg are combined in a laboratory dish, where fertilization occurs. The resulting embryo is then transferred to the woman's uterus (womb) to implant and develop naturally. Usually, 2-4 embryos are placed in the woman's uterus at one time. Each attempt is called a cycle. Other scientists had shown that egg cells from rabbits could be fertilized in test tubes when sperm was added, giving rise to offspring. It turned out that human eggs have an entirely different life cycle than those of rabbits. In a series of experimental studies conducted together with several different co-workers, Edwards made a number of fundamental discoveries. He clarified how human eggs mature, how

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Robert Edwards
A Nobel Laureate

The Nobel Prize in Physiology or Medicine for 2010 is awarded for the discoveries of *in-vitro fertilization*. Nobel panel lauded his "brilliant combination of basic and applied Medical research" and his ability to overcome various hurdles in "his persistence to discover a method that would help to alleviate problem of infertility". As the honour of being a Nobel laureate, Edwards has won 10 million Swedish kronor (\$1.5 million) for his contributions to "milestone in the development of modern medicine". He is a recipient of Fellow of the Royal Society, the Albert Lasker Clinical Medical Research Award, etc. and also known as a living genius.

different hormones regulate their maturation, and at which time point the eggs are susceptible to the fertilizing sperm⁷.⁸ He also determined the conditions under which sperm is activated and has the capacity to fertilize the egg. In 1969, his efforts met with success when, for the first time, human egg was fertilized in a test tube⁹. In spite of this success, a major problem remained. The fertilized egg did not develop beyond a single cell division. Edwards suspected that eggs that had matured in ovaries before they were removed for IVF would function better, and looked for possible ways to obtain such eggs in a safe way. By analyzing patients' hormone levels, it is possible to determine the best time point for fertilization and maximize the chances for success. In 1978, Lesley and John Brown came to the clinic after nine years of failed attempts to have a child. IVF treatment was carried out, and when the fertilized egg had developed into an embryo with 8 cells, it was returned to Mrs. Brown. A healthy baby, Louise Brown, was born through Caesarian section after a full-term pregnancy, on 25 July, 1978. IVF had moved from vision to reality and a new era in medicine had begun⁹.

Refinement in IVF

Edwards and Steptoe had established the Bourn Hall Clinic in Cambridge, the world's first centre for IVF therapy, where gynecologists and cell biologists from all around the world were trained to improve methods of IVF research. A majority of infertile women can now be able to conceive a baby as a result of IVF¹⁰.

With the advent of recent technological advances and researcher pool many of the world's scientists have been motivated and diverted to the field of reproductive biology. Today, IVF is an established therapy throughout the world. It has undergone several important improvements. For example, development of intra-cytoplasmic sperm injection (ICSI) involving microinjection of single sperm directly into the egg cell in culture dishes. This method has significantly improved the treatment of male infertility¹¹⁻¹³. Moreover, mature eggs suitable for IVF can be identified by ultrasound and removed with a fine syringe rather than through the

laparoscope. The IVF method also serves as the basis for development of preimplantation genetic diagnostics (PGD), i.e. a procedure performed in vitro on in vitro fertilized early embryo cells to reduce the risk that parents convey a severe genetic disorder or a chromosomal abnormality to their progeny¹⁴. IVF is comparatively safe and effective therapy. 20-30% of fertilized eggs lead to birth of a child. Complications include preterm births, but are very rare when one egg only is inserted into the mother. This could be explained by the older age of these women or by factors related to the underlying cause of their infertility. Long term follow-up studies have shown that IVF children are as healthy as other children^{15,16}. Louise Brown and several other IVF children have given birth to children themselves with no help of IVF. This is probably the best evidence for the safety and success of IVF therapy. Today, Robert Edwards' vision is a reality and brings joy to infertile people all over the world¹⁷.

IVF and Ethics

Ethical regulations are the most important part of any experimentation work involving animals and human population. After successful IVF therapy, Edward realized that there should be some strict ethical guidelines which every researcher have to understand and followed before practice. Since 1978 Edwards has participated actively in ethical and safety discussions and debates on human reproductive research¹⁸. Although IVF therapy was successful and safe in initial studies, Edward faced strong opposition from religious leaders commenting on morale issues, from government officials at that time who felt it was more imperative to limit population growth rather than to treat infertility and from scientific society that questions on embryo safety issues. In addition to this Edwards and Steptoe in 1971 had applied to the Medical Research Council (MRC) in the UK for long-term support in programmes of scientific and clinical 'Studies on Human Reproduction'. The MRC turned down to support the funding on ethical and safety grounds due to birth of abnormal babies¹⁹⁻²¹. But still he managed to continue research work with the donations from private sources.

Review Article

Conclusion

Although in the past IVF technique was a matter of controversy, nowadays it has become a routine mainstay in most of the developed nations. It had touch millions of lives and still helps to create millions. Keeping in the mind that future may rely more on IVF and we may hope for even better generations without inheriting several debilitating diseases, this pioneer work done by Sir Robert G. Edwards and co-workers is a much deserving invention not only for winning Nobel Prize but for succession of human race for the benefit of mankind.

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