

“Transfer of a Human Zygote” (1973), by David De Kretzer, Peter Dennis, Bryan Hudson, John Leeton, Alexander Lopata, Ken Outch, James Talbot, and Carl Wood

On 29 September 1973, researchers David De Kretzer, Peter Dennis, Bryan Hudson, John Leeton, Alexander Lopata, Ken Outch, James Talbot, and Carl Wood published “Transfer of a Human Zygote,” in *The Lancet*. In the article, the authors describe an experiment that resulted in one of the first pregnancies established via in vitro fertilization, or IVF. Prior to the article’s publication in 1973, there was no published evidence demonstrating whether IVF treatment would work in humans, although evidence existed showing that IVF worked in other mammals for breeding purposes. At the end of the article, the authors state that the embryo failed to implant into the wall of the patient’s uterus, leading to a miscarriage less than a week after the authors found evidence of pregnancy in the patient. The authors of “Transfer of a Human Zygote” were some of the first researchers to perform IVF, although unsuccessfully, which contributed to the overall understanding of IVF as an emerging technology.

The article “Transfer of a Human Zygote” is a short report describing an IVF experiment led by a team of IVF researchers from Australia in 1973. IVF is a medical procedure where scientists fertilize egg cells with sperm cells outside of a woman’s body, in a test tube or glass dish. After the sperm cell fertilizes the egg cell, which then begins to divide, embryonic development begins. The next step in the IVF procedure is to transfer the embryo from the sterile laboratory environment to the inside of the woman’s uterus, where it can implant and continue the early stages of embryonic development. The uterus is a female reproductive organ in which embryos develop into fetuses. While the goal of IVF is for the fertilized egg to implant in the uterus and result in a viable pregnancy, sometimes that does not happen. Because of that, scientists typically transfer several embryos to improve the possibility of producing a pregnancy.

The authors of the article worked together in affiliation with the Monash IVF team in Melbourne, Australia. Physicians Leeton and Wood established the Monash IVF team in 1971. The team also included De Kretzer, whose name is also sometimes spelled as De Kretser, Dennis, Hudson, Lopata, Outch, and Talbot, who were the other authors of the paper, “Transfer of a Human Zygote.” The members of the team had all studied developmental or reproductive science prior to the creation of the Monash IVF team.

In the article, which is formatted as a letter to the editor, the authors discuss the methods and outcomes of the overall experiment. First, they discuss the various medical complications that the female patient faced that led to her infertility, as well as why she and her husband decided to both become subjects in the experiment. Then, the authors describe their methods for collecting egg cells from the female patient and sperm cells from the patient’s husband. In the following five paragraphs, the authors describe their methods for egg cell fertilization and for transferring the fertilized egg into the patient’s uterus. The article ends with the authors’ documentation of changes in the patient’s hormone levels, namely the rise of hCG, which they used as an indication for evidence of pregnancy in the female patient.

In the first section of the article, the authors note previous medical complications that the female patient had which led to her infertility. The authors describe how the thirty-six year old woman had previously had her right ovary and right fallopian tube removed because of pelvic pain, and they

added that the woman also had a blockage in her left fallopian tube, making it difficult for an egg cell to release during ovulation. The complications ultimately led to the patient's inability to conceive children through intercourse alone, because poorly-functioning ovaries often cannot produce viable egg cells, and blocked or absent fallopian tubes mean any produced egg cells cannot reach the uterus for further development. Fallopian tubes are two tubes in the female reproductive system where egg cells are fertilized and then travel to the uterus, where they can eventually implant. Implantation is when pregnancy begins. The authors mention that they informed the patient and her husband of possible risks that could occur as a result of the IVF procedure. According to the Mayo Clinic, some of the risks of IVF include miscarriage, premature birth, low neonatal birth weight, and ectopic pregnancy, which is when an embryo implants outside of the uterus, typically in the fallopian tube. They state that the patient and her husband both owned and managed a dairy farm and were familiar with the IVF techniques used on animals in the early 1970s.

In the next part of the article, the authors describe the methods they used to collect the woman's egg cells and the man's sperm cells. For five days, the authors gave the patient clomiphene citrate, a drug used to stimulate the growth of egg cell production and the release of multiple egg cells during ovulation. In addition, the authors state that they injected the woman with a hormone, human chorionic gonadotrophin on the ninth day, approximately twenty-four hours prior to the surgery during which they collected her egg cells. Human chorionic gonadotrophin, or hCG, is a group of hormones that the body naturally produces during pregnancy. Those hormones enable the fertilized egg cell to attach to the uterine wall. The authors state that twenty-four hours later, the patient underwent an operation during which they successfully opened her left fallopian tube. That procedure allowed for the egg cell to travel down the left fallopian tube, into the uterus where implantation occurs.

After the operation, the authors state they successfully extracted one viable egg cell. The authors state that they kept the egg cell in fluid just above room temperature until they were ready to fertilize it with sperm cells collected from the patient's husband. The authors describe their process for preparing the semen, which is the fluid that contains sperm cells. They state that analysis of the semen showed a normal sperm count and motility, meaning that the patient's husband's sperm cells were capable of fertilizing the egg cell that was collected.

In the next section of the article, the authors provide methods for fertilizing the egg cell and for transferring the fertilized egg to the uterus. The authors mention that they soaked the egg cell in semen for four hours. By soaking the egg cell in semen, the sperm cells could attach on to the egg cell and eventually enable one sperm cell to fertilize the egg cell. Forty-nine hours after fertilizing the egg cell, the authors observed an embryo containing three cells. Sixty-seven hours after fertilization, the authors observed a fertilized embryo in an early stage. Shortly after that observation, they began the process to transfer the fertilized embryo to the patient's uterus. The authors state they gave the female patient pethidine, an opioid pain medication, and ritodrine, a medication that inhibits uterine activity. The authors then noted that they transferred the embryo into the woman's uterus via her vagina using an instrument shaped like a hollow tube.

In the last part of the article, the authors discuss the resulting pregnancy and miscarriage from the procedure, as well as advice for future IVF experiments. Eighteen days after the embryo was transferred to the uterus, the authors noted a rise in human chorionic gonadotrophin levels, which is something that researchers typically see when a woman is pregnant. They concluded the embryo had continued to grow and confirmed the woman was pregnant. Ten days after the patient's surgery to open her left fallopian tube, one of her external incision sites tore open and ruptured. The authors state they sutured the abdominal incision from the surgery but did not examine the uterus. Three days after the wound was repaired, the patient began menstruating, meaning that her body was naturally discharging the lining and blood from her uterus. That process occurs once a month and is typically a sign that a female is not pregnant. Therefore, the authors conclude that the patient must have had a miscarriage sometime before menstruation began.

While the IVF process proved successful, the pregnancy did ultimately end in a miscarriage shortly after the researchers transferred the embryo into the woman's uterus. However, the experiment opened up opportunities for further validation of potential IVF use in humans. In 1978 at the Royal Oldham Hospital in Oldham, England, five years "Transfer of a Human Zygote" was published, sci-

entists Patrick Steptoe and Robert Edwards organized an experiment that led to one of the world's first IVF-produced infants, Louise Brown, who is sometimes referred to as the world's first test-tube baby. By the early 1980s, medical providers started opening IVF clinics around the world as more people began using the IVF process to conceive children of their own. In 1990, only twelve years after Brown was born, there were 95,000 IVF live births reported around the world. In 2018, the number of live births jumped to over eight million children as a result of IVF treatment. Although the 1973 experiment led by De Kretzer, Dennis, Hudson, Leeton, Lopata, Outch, Talbot, and Wood ended in miscarriage, the article provided insight to researchers and the general public that IVF treatment was capable of treating infertility.

Sources

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