“Pregnancy Established in an Infertile Patient After Transfer of a Donated Embryo Fertilized

In 1983, researchers Alan Trounson, John Leeton, Carl Wood, Mandy Besanko, and Angelo Conti published the article “Pregnancy Established in an Infertile Patient After Transfer of a Donated Embryo Fertilized In Vitro” in The British Medical Journal. In the article, the authors discuss one of the first successful experiments using in vitro fertilization, or IVF, with the use of a human donor embryo at the Monash University and Queen Victoria Medical Center in Melbourne, Australia. Prior to the article’s publication, it was uncertain whether scientists could successfully use human donor embryos in IVF techniques. Although the pregnancy ended in a miscarriage ten weeks later, it showed that IVF was possible for those who needed to use someone else’s donated egg cells. Trounson and his colleagues’ paper provided a basis for future IVF pregnancies using donated embryos and helped develop a treatment option for men and women who could not conceive through sexual intercourse alone.

IVF is a medical procedure in which the fertilization of an egg cell by sperm occurs in a glass dish in a laboratory setting rather than in a woman’s body. The process of an IVF procedure using donated embryos begins when physicians give a fertile woman a drug and hormones in order to stimulate the production of multiple egg cells in the uterus. The physicians then remove several of those egg cells from her uterus and fertilize them with sperm cells, which produces an embryo. In the specific process of using donor eggs, a woman donates egg cells to another person.

Prior to the experiment, the authors questioned whether it was possible for an older woman who had no ovarian function to become pregnant with a donated egg cell fertilized in vitro, with the manipulation of an ovulatory stimulant drug and a group of hormones. At the time, successes in IVF research included IVF-donated embryo animal studies and Australia’s first IVF human births in 1978 by scientists Patrick Steptoe and Robert Edwards. Those achievements enabled the authors to further question the possibilities of IVF in humans.

The article is a short report of an IVF experiment led by authors Trounson, Leeton, Wood, Besanko, and Conti. In 1982, Trounson and his team began working on the IVF experiment in an attempt to treat women who were primarily around forty years of age and older and who had no ovarian function. Trounson, a physician who specialized in stem cell research at the time, was later the president of the California Institute for Regenerative Medicine in Oakland, California, from 2007 to 2014. From 1968 to 1987, Leeton was the director of the Infertility Clinic at Queen Victoria Medical Center. He established Australia’s first family planning clinic in 1967 in Melbourne, Australia, as well as Melbourne’s first donor sperm organization in 1969. From 1964 to 1992, Wood worked as a professor and chairman of Obstetrics and Gynecology at the Queen Victoria Medical Center at Monash University. At the time of the experiment, Besanko was a technical officer and Conti was a visiting research fellow.

The authors divide the article into three sections. In the first section, the authors describe their process for obtaining multiple egg cells from the donor. Furthermore, the authors note the patients’ rights as well as the options that donor women have if the physicians collect more than three egg cells from their uterus. In the second section, the authors mention general information about the donor, general information about the recipient, and describe their process of fertilizing and transferring the egg cells. In the third section of the paper, the authors explain possible reasons for the recipient’s miscarriage, and the ethical and legal issues surrounding the use of donor embryos in IVF procedures.

In the introduction, the authors discuss the general layout of the experiment. The authors state that they used a drug and a group of hormones to stimulate ovulation to occur in the donor. Ovulation is a process occurring in the female body during which an ovary releases one egg cell roughly ever twenty-eight days for fertilization. However, the authors stimulated ovulation in the donor with the use of a drug and a group of hormones that causes multiple egg cells to be released in a single month. The authors later harvested those eggs and fertilized them in a lab with sperm cells. Those fertilized eggs would later become embryos. The authors then state that their paper discussed a forty-two year old female donor, classified as patient A. They also included discussion of a thirty-eight year old female recipient, classified as patient B, in their paper.

In the methods section of their paper, the authors describe the patients involved in the experiment, as well as the methods that they used during the experiment. They begin by describing patient A and patient A's husband. The authors state that patient A's husband had a normal sperm count and motility, meaning he was able to produce healthy sperm to fertilize her eggs. The authors describe the patient as an infertile woman who had numerous medical complications such as a blocked left fallopian tube, a twisted right fallopian tube, and a three centimeter benign tumor attached to the uterine wall. Fallopian tubes are two tubes located in the female reproductive system where eggs are received from the ovaries and travel to the uterus. After giving patient A a variety of drugs to induce ovulation over a span of fourteen days, the authors were able to collect five egg cells from that patient.

Next, the authors describe patient B and patient B's husband. The authors state that patient B's husband had a complete absence of sperm, which meant that he carried no sperm that could successfully fertilize an egg cell. In addition, patient B herself presented with multiple medical complications. After six unsuccessful attempts of getting pregnant through artificial insemination, the authors found abnormal peritubal adhesions, or scar tissue that prevents an egg and sperm from coming together, on her left fallopian tube. The authors found a hole in her right fallopian tube, as well as a three centimeter benign tumor on the wall of patient B's uterus. A few years prior to the experiment, patient B underwent a surgery known as salpingolysis, or a procedure designed to remove scar tissue from fallopian tubes to provide a higher chance of successful ovulation.

The authors then describe their process for fertilizing the egg cells. The authors state that they obtained a semen sample, which is the fluid that contains sperm, from patient A's husband an hour before fertilization. The authors used the semen sample to fertilize four out of the five egg cells. Those four fertilized egg cells were for implanting in patient A's uterus, while the remaining unfertilized one egg cell was donated to patient B. Because patient B's husband was infertile, the authors used a frozen sample of semen containing identical physical characteristics as patient B's husband, such as race, hair and eye color, build, height, and blood type, to fertilize the last egg cell, which patient B would receive.

The authors note that twelve hours after fertilization, all five egg cells were successfully fertilized and had developed into embryos. Next, the authors describe their treatment and transfer of the embryos. They transferred the one egg cell that was fertilized by the frozen sample of semen to patient B's uterus. The authors transferred three out of the remaining four egg cells that were fertilized by patient A's husband's sperm to patient A.

At the end of the methods section, the authors discuss signs of pregnancy in patient B. Prior to the authors' transfer of embryos to patients A and B, they observed a large increase in hormone production between both patients. The authors indicate that that large increase in hormone production showed that the women were fully capable of sustaining the growth of embryos in their uteri. After transfer of the embryos to patients A and B, the authors obtained blood samples from both women to identify hormones associated with a successful pregnancy. They found that patient B was successfully pregnant, whereas patient A showed no signs of pregnancy.

However, the authors noted that ten weeks after the embryonic transfer, patient B began to notice minor vaginal bleeding. The authors measured a decrease in hormone levels in her body via a blood test that, when low, indicates that the woman's body is no longer sustaining the pregnancy. The authors concluded that patient B's pregnancy ended in an early miscarriage after ten weeks. They analyzed the miscarried fetus to gain further insight as to why the miscarriage happened and found

that the fetus had a trisomy of chromosome 9, a genetic disorder also known as mosaic trisomy 9. Normal chromosomes are found in pairs of two, and trisomies are chromosomes found in groups of threes, which are typically abnormal and potentially dangerous. Mosaic trisomy 9 is a rare genetic disorder that forms randomly during the formation of a fertilized egg or after fertilization takes place. It often leads to abnormalities such as structural deformities of the heart, growth deficiencies prior to birth, noticeable differences in the shape of the facial region and skull, and intellectual disabilities. Mosaic trisomy 9 occurs in approximately 2.5 percent of all spontaneous miscarriages. Most individuals born with the disorder will die within one year of age.

In the discussion, the authors report possible reasons for the miscarriage in patient B, explain why patient A did not become pregnant, and discuss ethical issues that had begun after the experiment was conducted. The miscarried fetus having mosaic trisomy 9 led the authors toward possible explanations for the miscarriage. In the experimental findings, the authors identified previous reports outside of IVF experiments in which pregnancies with embryos that had mosaic trisomy 9 showed that natural miscarriage often occurred between sixty-eight to 104 days in women aged twenty-seven years old and forty-two years old. In addition, the authors went on to note another possible explanation for the miscarriage, stating that patient B could have had an undiagnosed condition that could have caused genetic abnormalities in the egg cell. The authors then offer a possible explanation as to why patient A did not become pregnant even though they transferred three embryos to her uterus. They state it could have been due to the fact that they stimulated her ovulatory cycle with clomiphene citrate and gonadotropins, substances meant to increase hormone levels, in order to release multiple egg cells, which could have reduced the body's ability to sustain an embryo in patient A's uterus.

The authors also discuss some of the ethical issues that emerged after the experiment. They state that prior to the publication of the paper in 1983, the ethics committee of Queen Victoria Medical Center in Melbourne, Australia, permitted egg cell donation with the requirement that the donor and recipient's identifications remain anonymous. In response, concerns began over whether it was moral to eliminate any possibility for a donor-conceived child to know information about their genetic ancestors.

After the paper's publication in 1983, laws pertaining to donor-recipient confidentiality and anonymousness began to change in Australia. In 1988, the Victorian legislation in Australia passed a law enabling donor-conceived children or parents with younger children to request information about the donor as long as both parties consented. In 1995, the Infertility Treatment Act of 1995 was passed in Australia to strengthen donor-conceived individuals' rights by permitting requests to access information about their donor parents as soon as they reached legal adult age. However, in 2006, the National Accreditation Scheme permanently prohibited all anonymous donations of embryos, egg cells, or sperm within Australia.

Despite the early miscarriage in patient B, the paper marked one of the first successful attempts to transfer an embryo from a human donor to a human recipient. According to the authors, the fact that patient B was pregnant at all marked a new discovery for IVF researchers because it demonstrated that human females could become pregnant using egg cells donated by other women. It provided insight to the scientific community on successful techniques of IVF embryonic transfers between a donor and recipient who both had minimal to no typical ovarian function.

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