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## The Ethics of IVF

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## The Ethics of IVF

### Abstract

In vitro fertilization (IVF) has promised hope to many couples struggling with the pain of infertility. However, as with any new medical technology, the ethical implications of this procedure must be examined, particularly in light of recent events such as the birth of the first genetically modified human beings, made possible by IVF. It is crucial to examine oppositions to IVF based on principle, as well as address concerns related to adjacent issues such as the discard of unused embryos; the selection, payment, privacy, and parental rights of donors and surrogates; the importance of genetic parenthood; new combinations of gametes; preimplantation genetic diagnosis and selective implantation; and economic incentives. Short-term justifications shape long-term values, and so we must carefully consider the implications of IVF, even as we maintain compassion and grace toward couples dealing with the difficult realities of infertility.

### Keywords

ivf, in vitro fertilization, pgd, preimplantation, genetic, CRISPR, sperm donor, egg donor, surrogacy, reproductive, fertility, infertility, embryo, ethics, art, assisted reproductive technology, conception

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## Direction Determines Destination: The Ethics of IVF

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### Introduction

Since the birth of Louise Brown in 1978,<sup>1</sup> in vitro fertilization (IVF) has become a widely accepted infertility treatment option. It's an expensive and involved procedure, typically only sought out when other fertility therapies fail. By allowing fertilization to take place in a highly controlled environment using only healthy gametes, IVF gave hope to many couples who previously had no further recourse for treatment.

The IVF procedure takes place over several weeks, timed according to the would-be mother's menstrual cycle. Couples undergo a number of pre-cycle tests to identify any relevant factors that may influence treatment.<sup>2</sup> Treatment protocol often varies among individuals, but women wishing to conceive typically take birth control pills for several days or weeks before beginning a cycle in order to control cycle timing, follicle development, or other factors.

Once it is time for the treatment cycle to begin, ovulation is stimulated using gonadotropins and a gonadotropin-releasing hormone (GnRH) agonist or antagonist.<sup>3</sup> Gonadotropins are hormones that play a role in stimulating egg production in women; the GnRH agonist or antagonist prevents the dominant oocyte follicle(s) from being ovulated before the others have time to fully develop. This combination allows as many mature eggs as possible to be obtained.<sup>4</sup>

Next, the eggs must be retrieved from the ovaries. About 36 hours before the procedure, ovulation is induced by taking human chorionic gonadotropin. A needle is inserted up the vagina and through the vaginal wall to puncture the ovary. The follicular fluid is then extracted and taken to the laboratory to isolate the eggs. Usually, the patient is under anesthesia during this procedure.<sup>5</sup>

Once the eggs have been isolated, they are fertilized in vitro by either conventional fertilization or by intracytoplasmic sperm injection (ICSI). Under the conventional method, healthy sperm are isolated from the provided sample and simply exposed to the eggs for natural fertilization. ICSI involves manually injecting sperm into the egg, which may increase fertility rates, especially in cases of male-factor infertility.<sup>6</sup> ICSI is becoming an increasingly popular technique in many clinics; in 2012, more than three-quarters of

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<sup>1</sup> Craig Niederberger et al., "Forty Years of IVF," *Fertility and Sterility* 110 (2018), 185-324.

<sup>2</sup> Craig Niederberger et al., "Forty Years of IVF," *Fertility and Sterility* 110 (2018), 185-324.

<sup>3</sup> Artur Wdowiak, Edyta Wdowiak and Iwona Bojar, "Improving the Safety of the Embryo and the Patient during in Vitro Fertilization Procedures," *Wideochir Inne Tech Maloinwazyjne* 11 (2016), 137-143.

<sup>4</sup> Qiaohong Lai et al., "Comparison of the GnRH Agonist and Antagonist Protocol on the Same Patients in Assisted Reproduction during Controlled Ovarian Stimulation Cycles," *International Journal of Clinical and Experimental Pathology* 6 (2013), 1903-1910.

<sup>5</sup> Wdowiak, "Improving the Safety of the Embryo and the Patient during in Vitro Fertilization Procedures," , 137-143

<sup>6</sup> Craig Niederberger et al., "Forty Years of IVF," *Fertility and Sterility* 110 (2018), 185-324.

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all IVF procedures were performed using ICSI.<sup>7</sup> While some studies show that conventional fertilization may be preferred over ICSI in cases where male-factor fertility is not a concern,<sup>8</sup> others have found that ICSI has similar results in cases with unexplained infertility as in cases with male-factor infertility.<sup>9</sup>

The fertilized embryos are then cultured in an incubator until they can be transferred into the womb.<sup>10</sup> Embryos are allowed to grow for a few days in culture so they can be assessed for health and stability. Usually, only the one or two healthiest embryos are transferred to the womb in order to increase the chance of pregnancy; recently, many clinics have begun to particularly favor single-embryo transfer to reduce the risk of multiple births (twins, triplets, etc.). The unused embryos are then preserved for future cycles, donated for research, or discarded.<sup>11</sup>

To transfer the embryo(s), a special catheter is inserted up the vagina and into the uterus to inject the embryo into the endometrium, the lining of the uterus where the embryo will hopefully implant. The invasiveness of this procedure varies among individuals.<sup>12</sup> The fertility clinic typically follows up with the patient several times over the next few weeks until pregnancy can be determined, at which point care is transferred to the OB/GYN.

The success rate of IVF varies widely from individual to individual. One 2012 UK study found that overall, the chances of achieving live birth after the first cycle of IVF were 29.5%, with just over two-thirds of women achieving live birth after six cycles (a significant finding since IVF treatment is typically halted after just three or four cycles).<sup>13</sup>

In general, IVF outcomes worsen with age.<sup>14</sup> The 2016 National Summary Report of the Society for Assisted Reproductive Technology reported that women under the age of 35 had just under a 50% chance of conceiving for any given cycle; women aged 35-37 had a 34.8% chance; women aged 38-40 had a 21.8% chance, and women over 40 had a less than 10% chance.<sup>15</sup>

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<sup>7</sup> Hui Liu et al., "Conventional in Vitro Fertilization (IVF) Or Intracytoplasmic Sperm Injection (ICSI): Which is Preferred for Advanced Age Patients with Five Or Fewer Oocytes Retrieved?" *Archives of Gynecology and Obstetrics* 297 (2018), 1301-1306.

<sup>8</sup> Hui Liu et al., "Conventional in Vitro Fertilization (IVF) Or Intracytoplasmic Sperm Injection (ICSI): Which is Preferred for Advanced Age Patients with Five Or Fewer Oocytes Retrieved?" *Archives of Gynecology and Obstetrics* 297 (2018), 1301-1306.

<sup>9</sup> Wardah Alasmari et al., "Comparable Reproductive Outcomes of ICSI for Couples with Unexplained Infertility and Couples with Male Factor Infertility," 23 (2018), 393-398. Middle East Fertility Society Journal.

<sup>10</sup> Wdowiak, "Improving the Safety of the Embryo and the Patient during in Vitro Fertilization Procedures," , 137-143

<sup>11</sup> Niederberger, "Forty Years of IVF," , 185-324

<sup>12</sup> Wdowiak, "Improving the Safety of the Embryo and the Patient during in Vitro Fertilization Procedures," , 137-143

<sup>13</sup> Andrew Smith et al., "Live-Birth Rate Associated with Repeat in Vitro Fertilisation Treatment Cycles," *The Journal of the American Medical Association* 314 (2015), 2654-2662.

<sup>14</sup> Andrew Smith et al., "Live-Birth Rate Associated with Repeat in Vitro Fertilisation Treatment Cycles," *The Journal of the American Medical Association* 314 (2015), 2654-2662.

<sup>15</sup> (Niederberger and others 2018, 185-324).

IVF outcomes can also vary depending on whether one, two, or more embryos are transferred.<sup>16</sup> Transferring more embryos will increase the chances of a pregnancy, but is likely to result in twins or higher-order births.<sup>17</sup> Multiple birth is significantly more dangerous for the mother, with a high risk of complications and potential need for cesarean section delivery.<sup>18</sup>

Other physical risks of IVF include side effects of hormonal treatment, ovarian hyperstimulation syndrome during pre-treatment for egg retrieval,<sup>19</sup> infection from retrieval or transfer procedures,<sup>20</sup> and risks associated with pregnancy and delivery especially for older mothers.

This paper will briefly summarize some historical ethical criticisms of IVF as a practice in itself. The bulk of the paper will then address the ethical significance of issues adjacent to IVF, including the personhood of embryos, preimplantation genetic diagnosis, gamete donation, surrogacy, new gamete combinations, insurance incentives, and the role of biological children.

## IVF and ethical traditions

Some observers may oppose IVF *prima facie*, seeing any application of this technology as inherently unethical, even when used under the most conservative circumstances -- say, a heterosexual married couple for whom no other infertility treatment options are available, who only extract a few eggs from the wife and implant all embryos that result from fertilization with the husband's sperm. While this paper will primarily focus on adjacent issues of alternative applications, these objections are worth addressing at the outset.

The most common opposition to IVF in principle is based in natural law theory, which holds that "reason recognizes intrinsic goods persons seek for human fulfillment."<sup>21</sup> In other words, what is good can be logically deduced by observing what people naturally seek. This position was popularized by Thomas Aquinas and remains the predominant perspective of the Catholic church today.<sup>22</sup> The *Dignitas Personae*, a 2008 instruction from the Catholic Congregation for the Doctrine of the Faith, gives a representative overview of the Catholic natural law position on bioethical issues, including IVF. Like other Catholic documents (most notably the *Donum Vitae*), this declaration condemns IVF because it separates reproduction from sexual intercourse between the husband and wife, bringing a deeply personal act into the

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<sup>16</sup> V. E. Klenov, "Live Birth and Multiple Birth Rates in US in Vitro Fertilization Treatment using Donor Oocytes: A Comparison of Single-Embryo Transfer and Double-Embryo Transfer," *Journal of Assisted Reproduction and Genetics* 35 (2018), 1657-1664.

<sup>17</sup> Samer Tannus et al., "Cumulative Live Birth Rate Following Elective Single Blastocyst Transfer Compared with Double Blastocyst Transfer in Women Aged 40 Years and Over," *Reproductive BioMedicine Online* 35 (2017), 733-738.

<sup>18</sup> Ammon Goldworth, "The Ethics of in Vitro Fertilization," *Pediatrics in Review* 20 (1999), 28-31.

<sup>19</sup> Wdowiak, "Improving the Safety of the Embryo and the Patient during in Vitro Fertilization Procedures," 137-143

<sup>20</sup> Artur Wdowiak, Edyta Wdowiak and Iwona Bojar, "Improving the Safety of the Embryo and the Patient during in Vitro Fertilization Procedures," *Wideochir Inne Tech Maloinwazyjne* 11 (2016), 137-143.

<sup>21</sup> N. Steffen, "Core Values in Bioethics: A Natural Law Perspective," *Ethics, Medicine, and Public Health* 2 (2016), 170-180.

<sup>22</sup> D. A. Jones, "Christian Ethics, Roman Catholic," in *Encyclopedia of Applied Ethics, Second Edition*, ed. Ruth ChadwickElsevier, Inc., 2012), 435-444.

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cold environment of the laboratory. The church maintains this position both on spiritual grounds that uphold the sacrament of marriage and on natural grounds that insist that reproduction inherently is and ought to be exclusively tied to sexual intercourse between husband and wife.<sup>23</sup> The *Dignitas Personae* also specifically rejected the use of ICSI, the discard of unwanted embryos, the freezing of eggs and embryos, and preimplantation genetic diagnosis.

Similarly, bioethicist Gilbert Meilaender argued that the biological bond between parent and child is of moral significance because 1) human beings are embodied in nature, 2) reproduction is at least one part of the purpose of the sexual union of husband and wife, and 3) children are meant to be a manifestation of the marital union of love, not the result of rational calculation and a purchased procedure.<sup>24</sup> According to Meilaender, the introduction of third parties into the procreative process -- be they physicians, donors, or surrogates -- violates the sacred nature of reproduction, blurs lines of kinship and family ties, fails to embody the union of the parents, instrumentalizes the human body, and turns the child into a product which is made, not begotten.<sup>25</sup>

Others have opposed IVF on the grounds that it makes the child substitutable, a mere manufactured commodity. The child is sought as a means to fulfill the intended parents' desires, rather than an end-in-him/herself, violating the Kantian imperative. Bioethicist Robert George warned of this even outside the context of IVF: when considered rightly, children ought to be "treated by their parents, even in their conception, not as a means to their parents' ends, but as ends-in-themselves; not as objects of the desire or will of their parents, but as subjects whose fundamental interests as human beings are protected by the principles of justice and human rights: not as property, but as persons."<sup>26</sup>

These views and others oppose IVF on principled grounds, claiming that even in the most ideal circumstances, IVF comes with a great moral cost, however genuinely good the result. Many of these claims are legitimate concerns that bear consideration; whatever the benefit to the individual, IVF has and certainly will continue to influence the shape of society -- our values, our morality, and our metaphysical beliefs. Where we as a society have landed on this issue will inevitably inform our answers to questions yet to come.

This principle of present decisions shaping future values is worth keeping in mind as we explore adjacent issues in the rest of this paper: the filling-out of alternative applications to the 'most conservative' option described at the beginning of this section. Some are future projections likely just around the corner; many are presently practiced and crucially significant for our understanding of family, procreation, and humanity.

## Unused embryos and the beginning of life

The single most significant ethical issue when considering the morality of IVF is the personhood of unused embryos. Almost always, more eggs are extracted and fertilized than mature and are transferred, as

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<sup>23</sup> Congregation for the Doctrine of the Faith, "Dignitas Personae," (2008).

<sup>24</sup> Gilbert Meilaender, *Bioethics: A Primer for Christians*, 3rd ed. (Grand Rapids, Michigan: Eerdmans, 2013).

<sup>25</sup> Gilbert Meilaender, *Bioethics: A Primer for Christians*, 3rd ed. (Grand Rapids, Michigan: Eerdmans, 2013).

<sup>26</sup> (George )"

described above. This practice raises many significant ethical issues that have contributed to the abortion debate, still controversial in the U.S. nearly half a century after *Roe vs. Wade*.

Defining what makes a person a person has been the central question of bioethics since the discipline's beginning. In particular, the grey areas around birth and death have been the subject of both medical inquiry and philosophical contemplation. The definitive moment when a new person comes into existence has been argued to take place at conception, implantation, the point of brain development, the point at which the fetus can feel pain, the point at which the fetus would be viable outside the womb, and birth.

Marking that moment requires a sufficient definition of what qualities and/or capacities it is, exactly, that make a living thing a person. The state of New York decided this year that a baby is a person only if his/her mother wanted him/her to exist, repealing any protection for babies born alive after an abortion attempt. This implicitly affirmed a relational view of personhood, recognizing the humanity of the baby only if he/she is loved or wanted by someone else. While many celebrated the passing of this law, many others, including some who support abortion in other cases, mourned this legalization of infanticide.

Others, such as the utilitarian philosopher Peter Singer,<sup>27</sup> try to place personhood on a spectrum, often based on qualities such as intelligence, moral reasoning, consciousness, and/or self-awareness. This is troubling, however, since this definition necessitates that one adult human may be more of a "person" than another. Taken to Singer's extremes, some animals may be classified as more valuable than some children and mentally disabled people.

Attempts to mark the beginning of personhood as it relates to the human embryo face the challenge that while personhood should not be defined as a spectrum, development necessarily is. The brain develops over a period of time; sensitivity to pain likewise changes; viability is constantly being altered by changes in medical technology, while even a baby who is born alive is not viable without care.

Implantation and conception are the only two clearly distinguishable markers that don't constitute moving targets, and seem the only biologically defensible moral positions. Of the two, I tend to favor conception as the most likely moment for the creation of a new person for two reasons. First, when considering decisions such as selective embryo transfer or abortion, the outcome is one of two ethical extremes: it is either morally permissible or it is murder. Since the potential harm if we choose incorrectly is so vast, I consider the morally right decision to be the more conservative one. Second, implantation is a change in location from the fallopian tubes to the wall of the uterus, while conception is a change in being (from two haploid, end-stage gametes to a new, genetically unique diploid cell). Conception is the point at which a new member of the human species is created, and I think that while the concepts of a person and a genetic human are not necessarily identical, the two concepts can generally be treated as united for practical purposes.

While neither the implantation nor the conception view allows for traditional abortions, the distinction is significant when it comes to IVF. Discarded embryos are past the point of conception, but have not yet been implanted. As we move on to address other ethical issues surrounding IVF, it is crucial to remember that it is not only the interests of the infertile couple but also their created children that are at stake.

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<sup>27</sup> John Hymers, "Not a Modest Proposal: Peter Singer and the Definition of Person," *Ethical Perspectives* 6 (1999), 126-138.

## Donors, surrogates, and new combinations of gametes

Since IVF distances reproduction from the physical act of sex, it enables couples to conceive in ways no longer limited by anatomical practicalities. A summary of possible combinations of gamete donors and surrogates can be found in table 1. A full treatment of every possible situation is beyond the scope of this paper, as is the discussion of whether homosexual couples should become parents. Instead, I will briefly outline the IVF-specific issues associated with 1) gamete donation, 2) surrogacy, and 3) new combinations of gametes, eg. sperm + sperm and egg + egg.

BIOLOGICAL SEX		SPERM	EGG	WOMB	GENETIC OUTCOME
PARTNER 1: MALE PARTNER 2: FEMALE	1	PARTNER 1	PARTNER 2	PARTNER 2	PARTNERS 1 + 2 (SPERM + EGG)
	2	DONOR	PARTNER 2	PARTNER 2	PARTNER 2 ONLY
	3	PARTNER 1	DONOR	PARTNER 2	PARTNER 1 ONLY
	4	PARTNER 1	PARTNER 2	DONOR	PARTNERS 1 + 2 (SURROGATE)
	5	DONOR	DONOR	PARTNER 2	N/A (EMBRYO ADOPTION)
	6	PARTNER 1	DONOR	DONOR	PARTNER 1 ONLY
PARTNER 1: MALE PARTNER 2: MALE	7	PARTNERS 1 + 2	N/A	DONOR	PARTNERS 1 + 2 (SPERM + SPERM)
PARTNER 1: FEMALE PARTNER 2: FEMALE	8	DONOR	PARTNER 1 OR 2	PARTNER 1 OR 2	PARTNER 1 OR 2
	9	N/A	PARTNERS 1 + 2	PARTNER 1 OR 2	PARTNERS 1 + 2 (EGG + EGG)

Table 1. Possible gamete and surrogate combinations.

### Gamete donation

Artificial insemination using donor sperm has been practiced since at least the late 1800's,<sup>28</sup> and the first known egg donation occurred in Australia in 1983, just five years after the first IVF birth.<sup>29</sup> Gamete donation provides couples with poor gamete quality the possibility of obtaining a child who is at least partially related and who can be carried to term by the would-be mother. While common, this practice raises significant ethical and legal questions regarding the relationships among the donor, recipients, and offspring.

<sup>28</sup> Willem Ombelet and Johan Van Robays, "Artificial Insemination History: Hurdles and Milestones," *Facts, Views & Vision in ObGyn* 7 (2015), 137.

<sup>29</sup> Daniel Shapiro, "Payment to Egg Donors is the Best Way to Ensure Supply Meets Demand," *Best Practice & Research Clinical Obstetrics & Gynaecology* 53 (2018), 73-84.

In the United States, sperm donors can be paid up to \$125 per donation, depending on quality and/or quantity of usable sperm obtained.<sup>30</sup> Men with in-demand characteristics (including ethnicity, education, etc.) can be paid more.<sup>31</sup> Since the process for sperm donation is relatively simple, men can donate frequently, with some clinics offering up to \$1,000 to \$1,500 a month for frequent donors.<sup>32</sup>

On average, egg donors are paid up to \$10,000 or more,<sup>33</sup> but can donate only a few times at most, and have to undergo a fairly invasive procedure for extraction. Typically, egg donors undergo retrieval just as the would-be mother would in a non-donor IVF cycle: stimulation of ovulation followed by the in-clinic extraction procedure, with an average of about 13 eggs obtained. This does pose some risk of ovarian hyperstimulation syndrome and related side effects.<sup>34</sup>

The question of paying gamete donors at all has been a controversial one. In many ways, this practice reflects the growing trend of medical consumerism.<sup>35</sup> Some argue that paying donors commodifies reproduction and makes children into a mere product.<sup>36</sup> Others hold that given the time and, in the case of egg donors, risk and pain required to donate, it would be unjust for donors not to be compensated; further, sufficient high-quality gametes would not be available without incentivizing donation in some way.<sup>37</sup>

Also tied to the consumer trend in medicine is the question of whether couples should be permitted to choose the sperm/egg donor for their child. Typically, sperm banks collect various information about donors, biological and otherwise. Medical anthropologist Diane Tober describes a lesbian couple who described their sperm donor as “a doctor, 6 foot 4 inches, [who] played basketball and drank coffee.”<sup>38</sup> Medical information is always required for the sake of producing a healthy child, but donor profiles also often include secondary characteristics. For instance, recipients can choose a donor according to biological traits such as height, ethnicity, etc., as well as personal information like career, hobbies, and habits.

Both recipients and repositories select sperm donors based on a particular profile. As Tober observed, “Sperm donation, then, provides a window to reproductive values and a social/moral system, as well as the dynamics between culture and biology.” This practice seems to indicate that certain traits are valued more highly than others and worth selecting for when choosing how to produce a child (the same considerations apply in the case of egg donation). Often, recipients choose donors of the same ethnic and educational background as themselves.<sup>39</sup>

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<sup>30</sup> An Ravelingien et al., "Recipients' Views on Payment of Sperm Donors," *Reproductive BioMedicine Online* 31 (2015), 225-231.

<sup>31</sup> Diane Tober, "Semen as Gift, Semen as Goods: Reproductive Workers and the Market in Altruism," *Body and Society* 7 (2001), 137-160.

<sup>32</sup> Ravelingien, "Recipients' Views on Payment of Sperm Donors," , 225-231

<sup>33</sup> Shapiro, "Payment to Egg Donors is the Best Way to Ensure Supply Meets Demand," , 73-84

<sup>34</sup> Cynthia Cohen, "Reproductive Technologies: V. Gamete Donation," in *Encyclopedia of Bioethics*, 2004).

<sup>35</sup> Liz Meerabeau, "Consumerism and Health Care: The Example of Fertility Treatment," *Journal of Advanced Nursing* 27 (1998), 721-729.

<sup>36</sup> Meilaender, *Bioethics: A Primer for Christians*

<sup>37</sup> Shapiro, "Payment to Egg Donors is the Best Way to Ensure Supply Meets Demand," , 73-84

<sup>38</sup> Tober, "Semen as Gift, Semen as Goods: Reproductive Workers and the Market in Altruism," , 137-160

<sup>39</sup> Diane Tober, "Semen as Gift, Semen as Goods: Reproductive Workers and the Market in Altruism," *Body and Society* 7 (2001), 137-160.

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In traditional reproduction, an individual has the opportunity to select whom he or she would like to reproduce with; however, in most cases, selection is based on the desire for intimacy rather than to strategically produce an optimal child. In the minds of some, this leans dangerously close to eugenics. At the same time, however, the significance of producing a child with the genetic material of a stranger seems to warrant some amount of patient choice.

The anonymity of donors has historically been a toss-up when it comes to law. Anonymous donation is an established norm in many places, and protected by law in some countries including Spain, France, and Denmark. However, Norway, Sweden, the Netherlands, and the UK, among other countries, require donors to be identifiable to their potential genetic offspring.<sup>40</sup> Advocates of anonymity emphasize the protection of the donors' interest in privacy and the recipients' interest in providing what they believe to be the best care for their future child, not wanting to create doubt in his or her identity or weaken family ties. Critics, however, claim that children have a right to know where their genetic information comes from, and even seek out their genetic parent if they so choose. However, giving children this right is controversial in itself, even if donors are mandated to be identifiable. Donors typically don't see themselves as parents and don't wish to be thought of as bearing any responsibility to the offspring that are produced with their DNA.

Much of this discussion raises broader questions about the significance of genetics to family relationships and parenthood -- questions that never before demanded an answer, but that have already and will continue to be significant in the shaping of society, so long as family remains the building block of which it is made. This includes whether introducing a third party to the act of reproduction impacts a marriage, the significance of IVF over adoption when the child will ultimately only be partly related, and whether there is any obligation between parents and their genetic offspring.

## Surrogacy

While the concept of anonymity is out of the question, surrogacy deals with the same difficulties of compensation and selection as donation, magnified a hundredfold. While egg donation is a fairly invasive procedure, gestation is a far more intrusive burden on everyday life and demands a full three-quarters of a year.

Surrogacy removes not only conception, but childbearing itself from the context of the family. Sometimes, parents may have extra embryos left from previous failed IVF cycles, and choose to transfer to a surrogate instead of the intended mother with the hope of increasing the likelihood of pregnancy. However, in most cases when a surrogate is needed, only one of the intended parents can contribute genetic material at all. This raises even more questions about the role of genetics and family. What is the significance of biological children? If a child is going to be only 50% genetically related to the couple *and* will not be borne by the intended mother, what is the importance of conceiving this way as opposed to adoption? To what extent is the rise of surrogacy influenced by the broader trend of a desire for extreme control over the family-building process, and how far should that control be taken?

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<sup>40</sup> Immaculada De Melo-Martín, "How Best to Protect the Vital Interests of Donor-Conceived Individuals: Prohibiting Or Mandating Anonymity in Gamete Donations?" *Reproductive Biomedicine & Society Online* 3 (2016), 100-108.

## New combinations of gametes

Over the last few years, numerous studies have explored the possibility of new combinations of gametes to form an embryo, eliminating the need for either sperm or egg. For instance, in 2001, Australian scientists successfully injected somatic cells into mouse eggs to form embryos, although developmental viability was limited.<sup>41</sup> In 2016, scientists from the University of Bath demonstrated that parthenogenotes (unfertilized eggs that are tricked into developing like an embryo while remaining haploid) are capable of being fertilized by sperm; authors posited that any somatic cell with half its genetic material removed should be able to undergo the same process, removing the need for an egg.<sup>42</sup> In 2017, University of Cambridge scientists used embryonic mouse stem cells to mimic in-vitro embryogenesis.<sup>43</sup> In 2018, a study published in the journal *Nature* performed a similar process with human stem cells to produce a “blastocyst-like structure.”<sup>44</sup> If this technology were to be developed and popularized, the requirement for both male and female genetic parents could be eliminated, further changing the historically fundamental structure of family and kinship ties.

## Preimplantation genetic diagnosis and selective implantation

Preimplantation genetic diagnosis, or PGD, has been used in conjunction with IVF since 1990.<sup>45</sup> It's a form of genetic screening that allows physicians to detect monogenic (Mendelian) diseases, conditions which result from one or a very few mutations at known loci in the genome. Records are unclear on how common PGD is in the United States, but the practice is often recommended for couples with a history of genetic disease.<sup>46</sup>

### Background

DNA for PGD can be obtained at several stages of early development, including before the embryo is even formed. Polar bodies, the inert cells created alongside the egg during meiosis, can be safely removed and examined for aneuploidy,<sup>47</sup> the condition of having the incorrect number of chromosomes due to nondisjunction. Aneuploidy in a polar body often but not always indicates aneuploidy in the egg, which typically results in a failed pregnancy. This is a common problem for older women trying to conceive.<sup>48</sup> Examining polar bodies for some monogenic diseases has also been used to deduce the genotype of the egg with up to 97% accuracy.<sup>49</sup> Polar body biopsy may allow higher rates of pregnancy while avoiding some of

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<sup>41</sup> Orly Lacham-Kaplan, Rob Daniels and Alan Trounson, "Fertilization of Mouse Oocytes using Somatic Cells as Male Germ Cells," *Reproductive BioMedicine Online* 3 (2001), 205-211.

<sup>42</sup> Toru Suzuki et al., "Mice Produced by Mitotic Reprogramming of Sperm Injected into Haploid Parthenogenotes," *Nature Communications* 7 (2016), 1-15.

<sup>43</sup> Sarah Ellys Harrison et al., "Assembly of Embryonic and Extraembryonic Stem Cells to Mimic Embryogenesis in Vitro," *Science* 14 (2017).

<sup>44</sup> Nicolas Rivron et al., "Blastocyst-Like Structures Generated Solely from Stem Cells," *Nature* 557 (2018), 106-111.

<sup>45</sup> Niederberger, "Forty Years of IVF," , 185-324

<sup>46</sup> Susannah Baruch, David Kaufman and Kathy Hudson, "Genetic Testing of Embryos: Practices and Perspectives of US in Vitro Fertilization Clinics," *Fertility and Sterility* 89 (2008), 1053-1058.

<sup>47</sup> Markus Montag et al., "Polar Body Biopsy," *Fertility and Sterility* 3 (2013), 603-607.

<sup>48</sup> Marie MacLennan et al., "Oocyte Development, Meiosis and Aneuploidy," *Seminars in Cell and Developmental Biology* 45 (2015), 68-76.

<sup>49</sup> Karen Sermon, André Van Steirteghem and Inge Liebaers, "Preimplantation Genetic Diagnosis," *The Lancet* 363 (2004), 1633-1641.

the difficult ethical issues around personhood and conception, as polar bodies are not necessary for fertilization or embryonic development,<sup>50</sup> and any selection would occur before fertilization.

Polar body biopsy has its limitations, however. Since only the mother's genetic information is considered, it can only determine oocyte aneuploidy and, in some cases, recessive monogenic diseases. For recessive conditions, the father's genetic contribution could render the child either homozygously healthy or a heterozygous carrier, but as long as the dominant normal allele from the mother is present, the child should experience minimal ill effects. For dominant Mendelian conditions, however, a normal oocyte cannot guarantee a healthy child, as the father's allele alone could cause the full effects of the disease.

For this reason, other forms of genetic screening are often used instead of or in conjunction with polar body biopsy. Cleavage-stage biopsy allows embryos to grow in vitro for a few days until they reach their third division, when six or more cells are present. One or two cells are then extracted from each embryo for genetic examination. This typically involves polymerase chain reaction (PCR) amplification at the gene of interest followed by fluorescence in situ hybridization (FISH) to identify the presence or absence of a specific sequence. Cleavage-stage biopsy is the most common method of PGD,<sup>51</sup> since it allows direct examination at a variety of loci in the embryo itself, avoiding the major disadvantages of polar body biopsy. However, only one or two cells can be extracted, so accuracy may be compromised by chromosomal mosaicism and PCR sensitivity. There is little consensus on the best number of cells to extract, as extracting more cells gives greater diagnostic accuracy, but may reduce the embryo's ability to implant and develop normally.<sup>52</sup>

Some clinics have begun to increasingly use blastocyst biopsy as an alternative to cleavage-stage biopsy.<sup>53</sup> At this stage, the embryo consists of just over 100 cells, so more cells can be removed. This can lower the risk of PCR failure, which renders no result, or allele dropout, which gives incomplete results. However, only 36-66% of embryos mature this far in vitro.<sup>54</sup> Further, since embryos must be transferred to the womb within 5 or 6 days of extraction, blastocyst biopsy leaves little time for removal and diagnosis.<sup>55</sup>

Since cells are removed from the trophectoderm, a portion of the blastocyst that primarily contributes to the formation of placental tissue rather than the developing embryo, blastocyst biopsy is expected to have little effect on embryonic development.<sup>56</sup> In fact, one study found that while cleavage-stage biopsy resulted in a 39% decline in implantation outcomes relative to non-biopsied cells, while blastocyst (trophectoderm)

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<sup>50</sup> Montag, "Polar Body Biopsy," , 603-607

<sup>51</sup> C. Moutou et al., "ESHRE PGD Consortium Data Collection XII: Cycles from January to December 2009 with Pregnancy Follow-Up to October 2010," *Human Reproduction* 29 (2014), 880-903.

<sup>52</sup> Alan Thornhill, *Practice Manual of in Vitro Fertilization* (New York: Springer, 2012).

<sup>53</sup> Niederberger, "Forty Years of IVF," , 185-324

<sup>54</sup> G. Kokkali et al., "Blastocyst Biopsy Versus Cleavage Stage Biopsy and Blastocyst Transfer for Preimplantation Genetic Diagnosis of B-Thalassaemia: A Pilot Study," *Human Reproduction* 22 (2007), 1443-1449.

<sup>55</sup> Sermon, "Preimplantation Genetic Diagnosis," , 1633-1641

<sup>56</sup> Kokkali, "Blastocyst Biopsy Versus Cleavage Stage Biopsy and Blastocyst Transfer for Preimplantation Genetic Diagnosis of B-Thalassaemia: A Pilot Study," , 1443-1449

biopsy “had no meaningful impact on the developmental competence of the embryo as measured by implantation and delivery rates.”<sup>57</sup>

The comparatively high implantation failure of cleavage-stage biopsy for PGD is troubling on a practical level for those trying to conceive, as well as on a moral level if life begins at conception. However, polar body biopsy is limited in application and blastocyst biopsy faces challenges in both embryo survival and procedure completion time. Yet even if biopsy can be completed efficiently without harming the growing embryo, there are significant ethical questions surrounding the practice of PGD itself.

## Ethics

Clearly, to rid the world of genetic diseases would be an objectively good outcome. From a consequentialist perspective, this would avoid significant suffering due to genetic conditions. Further, it is possible that PGD by polar body biopsy could prevent abortions by enabling parents to only create children they are willing to carry to term. However, this raises the question of whether it is ever appropriate to select for certain traits when attempting to conceive offspring via IVF. There are three general categories to examine here: diagnosis of genetic diseases before fertilization, diagnosis of genetic diseases after fertilization, and selection for ‘non-medical’ traits.

First, since PGD by polar body biopsy occurs before fertilization, it avoids questions of personhood and gets at the simplest ethical question around medical genetic selection, namely, to what extent artificial selection among humans is ever acceptable. However, the relevance of this issue is diminished given the limited applications of polar body biopsy as addressed above. As such, a full treatment of this scenario is beyond the scope of this paper, but it is crucial to keep this central question in mind when looking at the following cases.

Second, PGD based on cleavage-stage or blastocyst biopsy may be problematic since selecting only healthy embryos to implant inevitably results in the discard of affected embryos. If life begins at conception, this is tantamount to murder, though the sterile and impressive environment of the laboratory obscures this reality. The discard of embryos also breaks the Kantian imperative to treat people as ends in themselves and never merely as means only. Though PGD is intended to provide the best life for a child by choosing a child who doesn’t suffer from genetic diseases, it may prematurely end the lives of those that do.

Further, while genetic diseases unfortunately cause significant suffering to many, it is also clear that many individuals affected by genetic diseases and disabilities live happy and productive lives. Some have argued that the normalization of PGD to select against embryos with genetic diseases and disabilities may cause further discrimination against and stigmatization of individuals with these conditions. It is also crucial to consider what conditions qualify to be treated as debilitating conditions eligible for PGD, as this technique could easily become a slippery slope into practical eugenics.

On the other hand, it is also interesting to consider the rare but real situations in which parents choose to implant the ‘affected’ embryo rather than the ‘normal’ one. For example, some deaf couples “regard deafness as a distinctive culture rather than a disability” and would prefer to raise a deaf child in that

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<sup>57</sup> Richard Scott et al., “Cleavage-Stage Biopsy significantly Impairs Human Embryonic Implantation Potential while Blastocyst Biopsy does Not: A Randomized and Paired Clinical Trial,” *Fertility and Sterility* 100 (2013), 624-630.

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community.<sup>58</sup> According to a 2008 study, when PGD was still a relatively young technology, 3% of IVF clinics offering PGD provided diagnoses for parents wishing to select *for* a genetic disease or disability,<sup>59</sup> a number that has undoubtedly increased in the eleven years since. Many raise here the child's right to an open future (unlimited by disability that can be avoided), but it is worth noting that parents already make many, many decisions on behalf of their children, making this a tricky line to draw.

Controversy has also arisen over parents using PGD to conceive a child who is an immunological match for an ill sibling. The human leukocyte antigen (HLA) complex is a series of genes that encode the major histocompatibility complex (MHC) proteins that mark the surface of a cell to identify it to the immune system. According to the aforementioned 2008 survey, 6% of IVF-PGD clinics have provided HLA typing to have a child who is a compatible donor for an existing child.<sup>60</sup> Typically, the stem cells from the child left in the umbilical cord -- usually discarded -- are harvested to be used to treat the older sibling,<sup>61</sup> meaning there is no physical trauma to the child during development or after birth.

Some are concerned by this situation, as the second child is seemingly brought into the world primarily to serve as a donor for the first, sometimes in cases in which parents were not planning to conceive an additional child. However, there is little available evidence that unplanned children are less loved generally; some have even argued that donor children should feel a sense of pride for having contributed in this way to the family. Critics see HLA typing as using a child as a means rather than an end, but others maintain that the Kantian imperative only prohibits using a person as a means *only*, and parents would typically see their second child -- even if not a part of their original plan -- as an end in him/herself as well. It is also worth considering that many parents in this situation would otherwise attempt to have a child to serve as a donor by natural birth; PGD in conjunction with IVF simply makes the match more likely. However, it is still crucial to remember that in this situation, the unused embryos are usually discarded, and the saving of one life doesn't outweigh the destruction of several others.

Finally, PGD is often used for sex selection. This can be for medical reasons, such as avoiding an X-linked disease, or simply to satisfy parental preference. Usually, preferential sex selection occurs when parents already have a child (or children) of one gender and wish for their next child to be the opposite gender. Sometimes, however, in cultures where children of one gender are considered of greater value, sex selection can be the product of outright discrimination. For this reason, many countries have outlawed non-medical sex selection; the United States is one of only a few countries that still allows this practice.<sup>62</sup>

Clearly, the slippery slope into non-medical applications of PGD is already becoming evident. As scientific understanding of the human genome has steadily increased over the last several decades, the capacity to select for non-medical traits has and will continue to grow. Further, the line between medical and non-medical traits is a blurry one, and, paradoxically, growing blurrier as our knowledge increases. Is selecting

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<sup>58</sup> Melissa Seymour Fahmy, "On the Supposed Moral Harm of Selecting for Deafness," *Bioethics* 25 (2011), 128-136.

<sup>59</sup> Baruch, "Genetic Testing of Embryos: Practices and Perspectives of US in Vitro Fertilization Clinics," 1053-1058

<sup>60</sup> Susannah Baruch, David Kaufman and Kathy Hudson, "Genetic Testing of Embryos: Practices and Perspectives of US in Vitro Fertilization Clinics," *Fertility and Sterility* 89 (2008), 1053-1058.

<sup>61</sup> Susannah Baruch, David Kaufman and Kathy Hudson, "Genetic Testing of Embryos: Practices and Perspectives of US in Vitro Fertilization Clinics," *Fertility and Sterility* 89 (2008), 1053-1058.

<sup>62</sup> Susannah Baruch, David Kaufman and Kathy Hudson, "Genetic Testing of Embryos: Practices and Perspectives of US in Vitro Fertilization Clinics," *Fertility and Sterility* 89 (2008), 1053-1058.

against a 70% increased risk of leukemia a medical treatment? What about 20%? What about genetic predispositions to mental illness such as depression? What about genetic factors that may be linked to violent behavior? What about superficial factors, such as height, that could lead to increased likelihood of bullying, which could result in anxiety?

While this level of specificity is currently in the future, it is not so far off as many suppose. In November 2018, Chinese researcher He Jiankui announced the birth of twin girls edited by CRISPR and implanted by IVF. This crossed the line of selection into the realm of engineering. While almost universally condemned by the scientific community, Jiankui's work opened the door to an inevitable future. CRISPR kits can be purchased on Amazon for less than \$200, and self-proclaimed 'biohackers' are already exploring its potential. This is no longer new and state-of-the-art technology. The question is only when it becomes acceptable in the professional as well as clandestine laboratory; it may be a matter of just a few years.

While CRISPR and other gene therapies bring their own set of ethical conundrums beyond the scope of this paper, it is crucial to consider where the technology is headed in order to clarify our thinking on what we have now. Concerns over modifications to the germ line, the line between medicine and preference, just distribution of resources, and the slippery slope into eugenics are all real, significant questions that should be answered before scientists like Jiankui answer them for us.

## Ethics of economy: IVF and insurance incentives

IVF is not only a complex and involved procedure, but an expensive one as well. Each cycle typically costs between \$10,000-\$15,000 out of pocket,<sup>63</sup> but the average couple has only a 29.5% chance of conceiving on the first cycle.<sup>64</sup> For hundreds of thousands of couples every year, it seems, the mere hope of conceiving a child is priceless -- or at least close enough to justify the cost. However, for many couples experiencing infertility, financial realities close the door to this possible treatment. Others have bankrupted themselves pursuing fruitless treatment, falling victim to the sunk-costs mentality that surely the *next* cycle would bring results. The pain of real financial barriers to conceiving children has led some to advocate for insurance coverage of advanced reproductive technologies (ART), including IVF.

Insurance coverage of ART is controversial -- not only because of the ethical issues involved, but also the complex policy decisions and compromises required in application. Infertility coverage isn't skimmed off the top of insurance company profits; it comes from either raising the cost of insurance for all participants or from reducing the coverage of other conditions. It's worth considering where the money comes from. Despite the very real emotional pain of infertility, is it a significant enough health condition to justify diverting funds from other medical treatments? On the other hand, is it just to restrict ART to those who can afford its steep price tag?

Nine U.S. states have mandated insurance coverage for IVF, reducing out-of-pocket costs to only about \$2,000-\$3,000 per cycle.<sup>65</sup> However, infertility coverage brings with it a knot of policy issues that have to

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<sup>63</sup> Barton Hamilton et al., "Health Care Access, Costs, and Treatment Dynamics: Evidence from in Vitro Fertilization," *American Economic Review*, no. 108 (2018), 3725-3777. <https://doi.org/10.1257/aer.20161014>.

<sup>64</sup> Smith, "Live-Birth Rate Associated with Repeat in Vitro Fertilisation Treatment Cycles," , 2654-2662

<sup>65</sup> Hamilton, "Health Care Access, Costs, and Treatment Dynamics: Evidence from in Vitro Fertilization," , 3725-3777

be untangled. What happens when insurer and patient interests collide over when and how treatment should be carried out? For example, since multiple embryos are often implanted at once to increase the chance of pregnancy, IVF births have significantly greater likelihood of twins, triplets, etc. compared to traditional pregnancy. In fact, IVF patients constitute more than half of all total multiple births.<sup>66</sup> While covered almost entirely by insurance, these multiple births cost four to sixteen times as much as single births even without including the cost of IVF,<sup>67</sup> and may cause significant health risks to the mother.<sup>68</sup> Patients, wanting to reduce costs and minimize invasive procedures, are more likely to pursue aggressive treatment and implant multiple embryos; insurers, wanting to save money in the long run, are more likely to advocate single implantation, even if it takes more cycles to achieve pregnancy. Innovative solutions to this quandary have been proposed, but this is just one of many unforeseen policy questions that will have to be answered by practitioners, lawmakers, and ethicists alike.

Concerns have also been raised over the commercial interests associated with IVF and other advanced reproductive technologies. For instance, feminist scholar Anne Donchin has criticized the role of fertility clinics, health care practitioners, and scientific researchers (all of whom have a financial stake in the use of IVF) in raising fears over the infertility ‘epidemic.’ Encouraging insurers and patients to consider infertility as a disease, in Donchin’s view, subtly leads couples struggling with infertility to consider themselves sick and in need of a cure, rather than fully considering all the options. This problem is compounded by the close ties that bind childbearing to family and identity, especially for women. Donchin writes,

Repeatedly, from physicians and other professionals with related interests, infertile women are urged to fulfill their "full reproductive potential" regardless of economic, psychological or bodily cost. ... The inability to produce a child at will, once deemed inevitable and accepted with resignation, is more likely to be regarded now as a surmountable impediment to personal self-fulfillment. Even adoption, once an obvious alternative for aspiring parents unable to conceive, is now more likely to be viewed as a last resort, to be pursued only after all medical approaches to the production of biologically related children have been exhausted.<sup>69</sup>

Some have even suggested that fertility clinics are incentivized to promote costly IVF procedures over less expensive alternatives that could equally or better serve the patient’s interests. The Australian clinic Monash IVF’s code of conduct explicitly states that clinicians should recognize that their primary obligation is to the company and its shareholders -- not to patients.<sup>70</sup> While this is a broader topic than IVF itself, spanning the rising trend toward medical consumerism, the fertility industry is particularly affected as a sector that is 1) relatively immature, 2) debatably not treating ‘disease’ per se, and 3) closely tied to very expensive and currently trendy treatment options.

It is worth carefully considering what kind of behavior we incentivize, and what those incentives say about our society and human ontology. How does IVF affect the relationships among patients, practitioners, and

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<sup>66</sup> Barton Hamilton et al., "Health Care Access, Costs, and Treatment Dynamics: Evidence from in Vitro Fertilization," *American Economic Review*, no. 108 (2018), 3725-3777. <https://doi.org/10.1257/aer.20161014>.

<sup>67</sup> Barton Hamilton et al., "Health Care Access, Costs, and Treatment Dynamics: Evidence from in Vitro Fertilization," *American Economic Review*, no. 108 (2018), 3725-3777. <https://doi.org/10.1257/aer.20161014>.

<sup>68</sup> Niederberger, "Forty Years of IVF," , 185-324

<sup>69</sup> Anne Donchin, "Health Care Access, Costs, and Treatment Dynamics: Evidence from in Vitro Fertilization," *Journal of Medicine and Philosophy* 21 (1996), 475-498.

<sup>70</sup> Christopher Mayes et al., "On the Fragility of Medical Virtue in a Neoliberal Context: The Case of Commercial Conflicts of Interest in Reproductive Medicine," *Theoretical Medicine and Bioethics* 37 (2016), 97-111.

insurers? If insurance covers IVF, should it also cover adoption? What does treating infertility as a disease say about the significance of reproduction? What is the role of biology in family?

## Conclusion

The pain of infertility is a difficult reality for many couples. IVF promises great hope as a new technology that surmounts barriers never before crossed. However, many see the moral cost of this technology as severe: not only does the normalization of IVF alter the metaphysical understanding of marriage, procreation, and family, it also results in the destruction of innumerable embryos every year, small human lives that are discarded as extra and unwanted. Selective implantation, the use of donors and surrogates, new combinations of gametes and somatic cells, PGD, CRISPR, and even the use of IVF itself may shift our sails toward stormy seas. Present decisions drive future developments; short-term justifications shape long-term values. Inertia is the enemy when direction determines destination.

IVF's promise provides powerful hope, and addressing this sensitive topic requires empathy, compassion, and grace. Yet as we seek solutions to the pain of infertility, let us beware of creating new problems we are unprepared to address. In answering medical questions, we cannot stop asking ethical ones.

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