Embryo Cryopreservation: Is Regulation Necessary?

J Hernandez, P Clark, A Borgia, A Butuc, J Haddad, S Lerner, D Odeh, M Patel

Citation

J Hernandez, P Clark, A Borgia, A Butuc, J Haddad, S Lerner, D Odeh, M Patel. *Embryo Cryopreservation: Is Regulation Necessary?*. The Internet Journal of Gynecology and Obstetrics. 2024 Volume 28 Number 1.

DOI: 10.5580/IJGO.57177

Abstract

The Dobbs v. Jackson ruling has reignited debate over a wide variety of subjects in reproductive health, particularly in assisted reproductive technologies (ART). With the matter of abortion now up to individual states, some legislators aim to severely restrict access to abortion by establishing fetal personhood–the concept that life begins at conception. This view aligns with that of the Roman Catholic Church. One of the most common forms of ART is in vitro fertilization (IVF), a manual procedure that combines sperm and egg to be planted in the uterus. IVF cycles often result in excess embryos, many resulting in indefinite storage. There are an estimated 900,000 to 1,000,000 spare embryos in storage today, often with no intended use for research or donation. This paper explores the ethical considerations surrounding spare embryos from a Catholic viewpoint, contending that the belief that life begins at conception justifies the conclusion that indefinite storage of these embryos constitutes a form of life support. Additionally, the paper analyzes the topic of frozen embryos from a medical, financial, and legal perspective.

INTRODUCTION:

Infertility has become a prevalent issue in today's society, with the World Health Organization reporting in 2023 that nearly 1 in 6 of the world's adult population experiences infertility, or roughly 17.5% of people worldwide [1]. Infertility is defined as the inability to become pregnant after 1 year of regular unprotected sex. Infertility occurs for a wide variety of reasons and can originate from one or both partners. This has created a high demand for

fertility services and other assisted reproductive technologies like in vitro fertilization (IVF), which represents more than "99% of ART procedures performed" in the United States [2]. Although the demand for IVF is high, costs for the service remain an issue for many. A single cycle of IVF can cost $20,000 dollars or more, making IVF an expensive procedure for those seeking infertility care. Furthermore, IVF often results in the cryopreservation of extra embryos, a process that not only comes with added expenses but also a wide range of legal and ethical concerns. Exact numbers are unknown, but current estimates put the number of these stored embryos at around 900,000 to 1,000,000. Indefinite storage has made the question of spare embryos' personhood (or lack thereof) a significant ethical concern. While some frozen embryos are selected for thawing/destruction, adoption, or scientific research, many others are left in indefinite storage. These options have multiple medical, legal, and ethical concerns for Roman Catholics.

Since the Dobbs v. Jackson ruling, several states have limited the availability of abortion, with others pursuing legislation that would establish fetal personhood laws to ban abortion altogether. The Roman Catholic Church argues that personhood begins right at conception, making IVF morally impermissible to many Catholics. For the spare embryos left in indefinite storage then, these remaining embryos exist in a state of limbo, holding the potential for life yet lingering in a state of unfulfilled existence. It is this ambiguous status of spare embryos that holds challenging moral connotations. If embryos are indeed persons, does that make indefinite storage a form of life support? Since these stored embryos lack a designated purpose (i.e. research or donation), what would be an ethical way of dealing with them? This paper explores the fragmented regulatory framework surrounding embryos, the substantial costs of IVF and storage, as well as the medical complexities of the IVF process. It then posits that if one accepts the premise of personhood beginning at conception, then indefinite storage of spare embryos can be thought of as an extraordinary means of life support, necessitating a merciful approach to their management.

CASE STUDY:

Along with the development of assisted reproductive technology (ART) has come a wide range of ethical and legal concerns, especially in situations involving oncofertility. In the case of Lisa, a 32-year-old married woman diagnosed with metastatic breast cancer, the dilemma surrounding the disposition of her remaining embryos highlights some of the wider ethical concerns that arise with prolonged storage [3]. Prior to Lisa's diagnosis and cancer treatment, Lisa sought out IVF and successfully banked nine embryos. Unfortunately, even after pursuing aggressive cancer treatment, Lisa still succumbed to her illness and her remaining embryos were left to her "husband's discretion". The husband could not come to a decision on what to do with the embryos and did "not wish to have the embryos placed in a gestational carrier, donate them to another couple, discard them, or continue paying for storage". The fertility clinic was unable to contact him [3]. The husbands' indecision as to how the embryos should be handled mirrors some of the available research on disposition. In a 2005 study of 58 couples, "after an average of 4.2 years of storage, 72% of couples with frozen embryos had not reached a disposition decision" [4]. A similar trend was found in a 2009 study, where an examination of 77 families found that 34% of the couples preferred indefinite storage, 22% preferred donation to science, 8% favored using the spare embryos for future attempts at conception, 6% preferred donation, and only 1% favored embryo destruction—with the remaining 29% not coming to a decision at all [5]. Another 2010 report of 1020 fertility patients in the U.S. discovered that "40% of patients who had completed childbearing could not identify a preferred disposition option for their excess embryos" and "one in five of those individuals indicated they were likely to put off the decision indefinitely" [6]. Because a considerable number of fertility patients demonstrate an inability to come to a final decision about their embryos, the banked embryos fall into a sort of 'limbo' where the embryos are left in indefinite storage. Although the ASRM outlines that it is reasonable to destroy embryos "if more than 5 years have passed since contact with the couple […] and no written instruction from the couple exists concerning disposition" – current estimates put the number of stored frozen embryos at around 900,000 to 1,000,000 [3] [7]. This suggests a general hesitance for some fertility patients to identify a fate for their embryos. Another factor known to contribute to embryos in indefinite storage is IVF clinics themselves, as many clinics feel "uncomfortable" with discarding embryos and gametes, instead choosing to "store abandoned embryos indefinitely insofar as they feel the embryos have intrinsic value" [3]. The growing number of spare embryos in the United States underlines a need for fertility clinics to make disposition decisions easier for their patients. State legislators may also consider laws which would put storage limits on abandoned embryos—albeit current debates surrounding fetal personhood could complicate the process.

LEGAL:

1. Fetal Personhood:

On June 24, 2022, the United States Supreme Court overturned Roe v. Wade, ruling in the case of Dobbs versus Jackson Women's Health Organization that the United States Constitution does not grant a right to abortion. This landmark decision returned the regulation of abortion to individual states, and 2023 saw twelve states (Alabama, Arkansas, Idaho, Kentucky, Louisiana, Mississippi, Missouri, Oklahoma, South Dakota, Tennessee, Texas, and West Virginia) enact a near total ban on abortion, while two others (North Dakota and Wisconsin) saw an unenforced ban [8]. Since the ruling, a growing number of states have drafted laws with a more uncompromising method of restricting abortion, limiting the practice by establishing fetal personhood. In Roe v. Wade, Supreme Court Justice Harry Blackmun famously wrote in an opinion against the Texas statute that "the word 'person,' as used in the Fourteenth Amendment, does not include the unborn" [9]. Five decades later with Roe v. Wade overturned, fetal personhood pundits oppose this interpretation, aiming to assign the legal rights given to people and extend them to pre-viable fetuses.

Fetal personhood laws have gained surprising traction since the ruling. The Guttmacher Institute's legislation tracker shows that the number of bills introduced to ban abortion by "establishing fetal personhood" has risen from five in 2023 to twenty-three in 2024 [10]. While none of these bills have passed in the state legislature yet, one recent case in Alabama has highlighted the complications fetal personhood interpretations can have on IVF treatments. On February 16, 2024, Alabama's Supreme Court ruled in a set of wrongful death cases that "an 1872 state law allowing parents to sue over the death of a minor child 'applies to all unborn children, regardless of their location'" [11]. The case involved three couples who had their "frozen embryos destroyed in an accident at a fertility clinic" [11]. Fearing criminal prosecution if the embryos were damaged, IVF

clinics in Alabama shut down for about three weeks, only reopening after state legislators passed a bill "granting civil and criminal immunity for in vitro fertilization service providers and receivers" [12]. Although Alabama is not the first to establish fetal personhood laws into legislation (and many states have fetal homicide provisions), Alabama's Supreme Court's decision highlights the legal ambiguity of fetuses in the United States. The most apparent example of this is in the Dobbs v. Jackson case itself, where Supreme Court Justice Alito writes, "Our opinion is not based on any view about if and when prenatal life is entitled to any of the rights enjoyed after birth" [13].

Despite a lack of federal standards on fetal personhood, some state legislatures have not abstained from embracing forms of it when "bringing criminal charges after miscarriage or stillbirth" [14]. Since 1999, the Marshall Project reports that over fifty women have been tried for child neglect or manslaughter because they "tested positive for drug use after a miscarriage or stillbirth" [14]. Some women without a history of drug abuse have found themselves under investigation, as shown by the case of Brittany Watts, an Ohio woman recently acquitted of "abuse of a corpse" when she elected to dispose of her nonviable fetus in 2023 after a miscarriage [15]. A similar prosecution was brought against Marshae Jones, an Alabamian woman accused of manslaughter after being shot in the abdomen during an altercation with another woman while five months pregnant, resulting in miscarriage [16]. The case was dropped and not brought to trial [16].

The legal status of fetuses is ambiguous nationwide, and this ambiguity appears to translate into the general public's point of view. Polls confirm that in the West, most people support access to abortion but will mourn a miscarriage and be outraged at the "murder of an early fetus during a violent attack on a pregnant person" [17]. In the United States especially, the lack of consistency in both the general public and legislation brings up another point of debate in IVF, the embryos' debated status as persons or property.

2. Persons or Property?

In the United States, "legislated limits on embryo cryostorage or mandate embryo disposition" are left to the decisions of patients and clinics with help from internal and professional guidelines [18]. This lack of federal regulation has created variation in the handling of frozen embryos in divorce cases, causing legal confusion as to whether embryos should be treated as marital property or entities beholden to state custody laws for children. Because of the nature of IVF itself (which typically results in cryopreservation of excess embryos), embryos can become part of property disputes should a couple divorce. This causes a recurring problem in U.S. courts, as these cases "seem to pit one partner's right to procreate against the other's right not to procreate" [19]. As of 2024, there is no consensus within the U.S. regarding the legal status of embryos. While states like New York, Colorado, and Iowa have declined to recognize pre-implanted embryos as persons, other states such as Tennessee, grant embryos a sort of "interim" status, with more rights than an object but less than an actual person [20]. One of the first cases to showcase this idea was Davis v. Davis. On June 1, 1992, the Tennessee Supreme Court ruled in favor of Junior Lewis Davis, a man who requested the cryopreserved embryos from a former marriage be "destroyed over the objections of his former wife, Mary Sue Davis" [21]. While the Tennessee Supreme Court agreed with the Court of Appeals that the embryos lacked personhood, the Tennessee Supreme Court also thought that the Court of Appeals went "too far" in treating the embryos as property [21]. Instead, the Tennessee Supreme Court opted for a sort of 'middle ground'—announcing that preserved embryos belong to a "category that entitles them to special respect because of their potential for human life" [21]. Although a 'middle ground' exists in the legal system, other states (such as Louisiana), grant embryos "a status equal to that of a living child, making the intentional destruction of frozen embryos illegal and punishable under law" [22]. Should Louisiana's take on the status of embryos become prevalent in the United States, the exact outcomes on IVF are unknown. Nonetheless, the Alabama Supreme Court's ruling in February and its unintended consequences on IVF is an expression of a budding fetal personhood movement in the U.S legal system.

FINANCIAL:

In 2014, the average cost of a single cycle of IVF was $12,513, with ICSI tacking on an additional $1,626 [23]. Accounting for inflation and variation in prices between clinics can put the actual cost to upwards of $20,000; however, this estimate does not always include storage and maintenance fees. Storage costs for frozen embryos vary but typically range from $300 to $600 per year per batch of embryos. Over several years, these costs can accumulate substantially [24]. In addition to the high consumer cost of cryopreservation, long term storage of embryos can be a major cost to cryopreservative companies themselves. Liquid nitrogen tanks, routine servicing of equipment,

environmental controls for temperature integrity, constant staffing, and security parameters to protect the stored embryos' viability are all factors which make maintenance costly for companies. Furthermore, it is difficult for storage facilities to have an exact gauge on how long an embryo will be stored, as it is based on the customer's desires and preferences. Such scenarios become of particular concern when patients stop paying storage fees. While there have been efforts in other nations such as Denmark, the United Kingdom, parts of Australia, and New Zealand to legislate limits to cryostorage to five or ten years, this is not the case in the United States [25]. Even with informed consent forms which "stipulate that nonpayment of storage fees would lead to discarding of their reproductive cells", storage facilities rarely follow this rule "for obvious reasons" [25]. Indeed, one 2016 study found that length of storage proved as a "risk factor for abandonment" with each year of paid cryostorage raising the risk of embryo abandonment by more than 7% [25].

Despite IVF being a major expense for fertility patients, most people end up paying the whole cost of fertility treatment out of pocket [24]. Very few private insurance companies cover fertility services, since fertility treatments are considered medically unnecessary. Only 19 states have laws in effect which cover some parts of fertility treatment, but this coverage usually only applies to fertility drugs and evaluations. Smaller employers were less likely than larger employers to "include fertility benefits in their employer-sponsored health plans", and the 2017 National Survey of Employer-Sponsored Health Plans showed that "56% of employers with 500 or more employees cover some type of fertility service, but most do not cover treatments such as IVF, IUI, or egg freezing" [24]. Public coverage of fertility treatment is even more limited. For most states, Medicaid coverage for diagnosis and actual fertility treatment is optional. The only state to have some form of provision for both infertility diagnostics and treatments is New York [24]. With most states offering little to no coverage for fertility services, procedures like IVF remain a heavy financial burden for most Americans. Future policies should consider expanded fertility coverage in insurance packages to reduce this expense for the public.

MEDICAL ANALYSIS:

1. The IVF process, Cryopreservation/freezing process, and storage/thawing process)

IVF, or in-vitro fertilization, is one of the most common forms of infertility treatment available. Female patients with tubo-peritoneal disease such as pelvic inflammatory disease and endometriosis are some indications for the use of assisted reproductive technologies such as IVF to achieve pregnancy [26]. Additionally, women who desire to have children but have comorbid conditions such as cancer that require treatment that are gonadotoxic may use IVF to store embryos and achieve pregnancy. Women who will undergo chemotherapy and/or radiation can cryopreserve their oocytes or embryos prior to treatment and transfer them after completion of chemotherapy [26] [27]. There is no established absolute contraindication for undergoing IVF; however, there are published guidelines and recommendations that advise against IVF in women with Marfan Syndrome, advanced heart failure, or with structural heart defects such as valvular stenosis and coarctation of aorta [26]. These conditions pose a threat to the embryo and the patient due to the increased physiological demand of pregnancy. Prior to IVF, patients undergo several evaluations to determine ovarian reserve and function through the assessment of their FSH, LH, and estradiol levels. Anti-Mullerian hormone or follicle counts can also be used as supplemental markers of ovarian reserve. After determination of ovarian reserve, pelvic imaging is done to evaluate for anatomical or structural abnormalities in the ovaries, fallopian tubes, and uterus that may hinder IVF success. Male partners also undergo semen analysis to evaluate morphological or motility issues causing infertility [26].

The goal of oocyte retrieval is to obtain multiple oocytes from one IVF cycle [26]. Considering that the natural cycle produces one or two oocytes, the ability to retrieve multiple oocytes increases the likelihood of achieving pregnancy [28]. IVF begins with ovarian stimulation using two established main protocols: the GnRH long agonist protocol and GnRH antagonist protocol. In general, these IVF protocols use injectable gonadotropins (FSH and LH) followed by human chorionic gonadotropin or hCG to promote follicular development and maturation within the ovarian oocytes [28]. The long GnRH agonist protocol involves administering GnRH agonists (such as triptorelin) daily, starting day 21 of the previous cycle, followed by gonadotropin daily starting on cycle day 2 of the subsequent cycle. GnRH agonist and gonadotropin are administered at the start of injections with hCG, which can be done 14 days post GNRH agonist regimen or when the ovarian follicles are 16 to 18 mm [29]. In the GnRH antagonist protocol, daily administration of gonadotropin on cycle day 2 or 3

with varied dosage depending on the size of ovarian follicles [29]. At around cycle day 6 of gonadotropin administration or when follicles reach 14 mm or more, subcutaneous administration of GnRH antagonists, such as cetrorelix) is begun [29]. After 14 days of initiation of therapy or when follicles are 16 to 18 mm, hCG is started. For both protocols, oocytes are retrieved after 34 to 36 hours of hCG injection. Progesterone is started either at the retrieval of oocytes or embryo transfer to ensure implantation and progression of pregnancy [26].

The next step in the process involves the retrieval of the oocyte. Early in the history of IVF, oocyte retrieval was done laparoscopically which posed difficulties due to it being time consuming, requirement of general anesthesia, and high cost [27]. With the development of ultrasound imaging and capacity for real-time imaging came with the ability to retrieve oocytes under ultrasound guidance. Ultrasound guided oocyte retrieval is now the gold standard method due in part because it is a safe and simple method. Transvaginal ultrasound guided follicular aspiration uses a needle introduced through the vaginal side wall and into the ovary. This occurs between 34 to 36 hours after ovarian stimulation. IV sedation is used for anesthesia and collection media is warmed to body temperature and kept at a physiological pH [30].

Insemination in conventional IVF involves the oocyte mixing with purified sperm or mechanical insertion of sperm into the oocyte [30]. Intracytoplasmic sperm injection is the method used for mechanical insertion of individual sperm into the oocyte and is the preferred insemination protocol [27]. This method is especially beneficial for the treatment of patients with male factor infertility [27]. Fertilization is confirmed by observation of 2 pronuclei in the zygote at 16-18 hours after insemination [30]. Embryos are kept in a culture medium (clinically known as simplex optimized medium and global medium) with careful consideration of temperature, pH, and oxygen levels to achieve the desired clinical outcome [27]. Embryos undergo morphological review and preimplantation genetic testing for ideal embryo selection prior to transfer [27].

Lastly, embryo transfer is done at 3 days following fertilization (cleavage stage) or at 5 days following fertilization (blastocyst stage). There are many advantages with transferring the embryo during the blastocyst stage, such as higher likelihood of live birth per cycle and fewer embryos needed to be used to achieve pregnancy [26]. Nadieberger et al. highlighted the importance of embryo transfer at the blastocyst stage in human IVF, which includes reduction of uterine contractions with day 5 embryos which can reduce embryo expulsion, capacity for optimal embryo selection through quantifying of embryo components such as the inner cell mass and trophectoderm, increased rates of implantation, reduced pregnancy timing, and facilitation of single embryo transfer which reduces the likelihood of multiple births and complications that can arise from it. Embryo transfer is done via transabdominal ultrasound guided catheter passing through the cervix [27]. Catheters may come in different sizes, diameters, lengths, and even degrees of visibility under ultrasound [27]. Proper guidance and placement of the catheter is essential in providing successful embryo transfer [27]. The catheter tip containing the embryo is placed close to the uterine fundus to achieve proper implantation with distances ranging between 5 to 27 mm from fundus [27]. Transfer medium using patient's serum, adherence compounds, and infusion of hCG into the uterine cavity can be done to potentially improve outcomes of embryo transfer and placement [27]. Consideration must also be taken in the speed of embryo injection due to concerns for embryo trauma. Excess embryos are then kept in cryopreservation for future use. In summary, key elements highlighted by Nadieberger et al. for-embryo transfer includes the selection of post-thaw embryo at the blastocyst stage, careful catheter loading, control of temperature and pH, use of ultrasound guided soft catheter, and slow injection 1.5 cm from the uterine fundus.

2. Cryopreservation

Embryo cryopreservation has advanced IVF by allowing storage of extra embryos for future use and led to the development of commercial donor egg banks [27] [30]. Cryopreservation refers to storing embryos at low temperatures with liquid nitrogen [28]. Cryopreservation can be done at several stages in the development process (zygote, cleavage stage, or blastocyst stage) with some studies showing better outcomes with cryopreserved embryos at either the zygote or blastocyst stage [31] [32].

There are currently two methods for the cryopreservation of human embryos: slow freezing and vitrification [33]. Initially, slow freezing was the predominant method but as advancements in reproductive technologies have been made there has been a shift to using vitrification as the preferred method [32]. Both methods use similar chemicals with differences being in the concentrations of chemicals used and cooling/warming rates [32]. Slow freezing uses low concentrations of cryoprotectant, low cooling rates, and fast

warming rates while vitrification uses high concentrations of cryoprotectant, ultrafast cooling rate, and ultrafast warming rates. With slow freezing, the embryo undergoes a process of rapid cooling to –7 degrees Celsius in a cryoprotectant medium (such as glycerol). The embryo then undergoes a consistent slow cooling period at rates of –0.3 to –1 degree Celsius per minute to reach a desired temperature range of –40 to –70 degrees Celsius at which point it is submerged into liquid nitrogen to achieve vitrification [33].

Vitrification is generally defined as the solidification of a watery solution without ice by directly converting liquid into a solid. Vitrification of embryos involves high concentrations of cryoprotectants and rapid cooling and warming rates. There are several different vitrification protocols that differ in the type of cryoprotectant used, cooling, storing, and warming methods [33]. One of the most common cryoprotectants used is a combination of 15% DMSO, 15% ethylene glycol, and 0.5 sucrose. Similar to the slow freezing method, liquid nitrogen is used in the cooling process at rates of –20 degrees Celsius per minute. To achieve ultrafast cooling rates, there are open embryo carriers designed to allow for the direct contact of embryos containing medium with liquid nitrogen [32]. Despite vitrification requiring high concentrations of cryoprotectant which then can damage embryos by osmotic stress or cellular toxicity, it has been shown to be the best strategy for cryopreservation at all stages of development [33].

The thawing process of cryopreserved embryos poses risks if warming and thawing is done too quickly. Cell damage can occur through the formation of ice crystals, so the warming rate for slow freezing and vitrification during thawing is rapid. The likelihood of successful implantation and thus pregnancy is based upon the quality of the embryo after it thaws. As stated above, both the slow freeze and vitrification methods use rapid warming rates in the thawing process. The slow freeze method uses decreasing concentrations of cryoprotectant at room temperature to achieve while vitrification undergoes rapid thawing at 37 degrees Celsius [34].

IVF rates have increased in recent years and estimates suggest that assisted reproductive technologies will contribute to 3% of the total world population by the next century [35]. These projections are based on the technological advancements in IVF and reproductive technologies. These include the application of microfluidics in IVF, which can automate procedures and reduce variability and the incorporation of artificial intelligence in IVF laboratories which has the potential for automation and standardization [36] [37].

Microfluidics is used primarily for the downsizing and simplifying laboratory techniques and is based on chips, microchannels, and chambers. Polymers, such as poly(dimethyl siloxane), known as PDMS, have shown good biocompatibility with human cells and tissues such as oocytes and sperm. The process of developing a microfluidic device is simple and cost effective and microfluidics can be used in every step of the IVF process [38]. Microfluidics can aid with storing, transferring, and insemination of embryos thereby reducing environmental stress and technician error [38]. It can provide better accuracy and improved efficiency in cases of male infertility by helping concentrate sperm [38].

Use of artificial intelligence (AI) has now opened the door for optimizing infertility treatment through the selection process. AI is being used for embryo grading (at the blastocyst stage) through radiology and pathology applications image models. With blastocyst grading and the selection of optimal embryos, these AI models can select the “fittest” embryos which would theoretically lead to higher rates of implantation. Application of neural frameworks for selecting of embryos in mice models has been done with a great deal of accuracy giving the hope that this could be applied to human embryo implantation at a large scale [39]. VerMilyea et al. used an AI based model that was trained to select embryos based on light microscopy images as compared to embryologists’ traditional methods of morphology grading methods. The AI model has a better predictive ability for evaluation of an embryo than traditional methods which can lead to the potential to standardize selection methods for embryos across multiple clinical environments.

In sperm selection analysis, various computer-based models are used for research and routine analysis of human and animal sperm. Application of these computer models with the addition of biometrics such as a person’s height, testicular volume, hormone levels, and volume of sperm at the time of ejaculation was able to retroactively predict chromosomal abnormalities with a high degree of accuracy [36]. AI can be used in mass data collection and network linkages. Data mining using AI would keep large scale data sets up to date. Data gathered could be used for the creation of models for diagnostic and prognostic purposes that clinicians can use for clinical decision making en masse or tailoring management as seen fit [36]. Data driven

approaches with the aid of AI would in turn lead to more evidence-based approaches by clinicians for more tailored and precise clinical decisions. The development of stem cell technology for use in IVF has culminated with the production of mature oocytes from induced pluripotent stem cells. The process, developed by Japanese scientists in 2016, involves the reprogramming of mouse tail skin cells into stem cells which then in turn are made to be oocytes [40]. This highlighted the possibility that in-vitro gametogenesis (IVG) in mammals is attainable. However, the process is known to be difficult to consistently replicate. Stem cell technology may offer the elimination of the oocyte retrieval step, further increasing the efficiency of the IVF process for the future.

(The following ethical analysis is reproduced without change from "Cryopreserved Embryos: A Catholic Alternative to Embryonic Stem Cell Research and Adoption", published 2011)

ETHICAL ANALYSIS:

Ethically, the concern about spare embryos focuses on the issue of personhood. If embryos are persons, then it would be a moral imperative to "rescue" these embryos from their current status of being in "frozen animation." Numerous ethicists, embryologists, legal professionals and specifically, the Roman Catholic Church, argue that personhood begins at conception or what is known as fertilization. Prior to fertilization we have two human gametes—sperm and egg, that are living but are not a living organism. When fertilization occurs, something human and living "in a different sense comes into being" [41]. Embryologists argue that "human development begins at fertilization when a male gamete or sperm (spermatozoon) unites with a female gamete or oocyte (ovum) to form a single cell—zygote. This highly specialized, totipotent cell marked the beginning of each of us as a unique individual" [42]. The Catholic Church teaches that "human life must be absolutely respected and protected from the moment of conception" [43]. "Right from fertilization is begun the adventure of a human life, and each of its great capacities requires time. . .to find its place and to be in a position to act. This teaching remains valid and is further confirmed, if confirmation were needed, by recent findings of human biological science which recognize that in the zygote resulting from fertilization the biological identity of a new human individual is already constituted" [44] The Church argues that at fertilization there is a new genetic individual in its own right, one who is whole, bodily, self-organizing, and genetically distinct from his or her mother and father [45]. Those who argue that personhood begins at fertilization would also argue that there is a moral imperative to give these frozen embryos the opportunity to be born and to develop because they are persons. Ethicist Therese Lysaught believes that embryo donation/adoption is an act that can properly be described as "rescuing a child orphaned before birth" [46]. Ethicists arguing for the "rescue" of these children would encourage women to implant these embryos in their wombs in order to bring them to term. Some would permit not only married women to do this but also single women and even lesbian couples. The moral principle of sanctity of human life would overcome any other moral considerations. However, not all, even in the Catholic Church, would agree to this ethical analysis. Opponents of this position argue that this would amount to material cooperation in an objective immoral action. Not only is the process of IVF considered an intrinsic moral evil by the Magisterium of the Catholic Church, but allowing for the donation/adoption of these embryos might condone the objective immoral procedure and may even encourage the creation of additional embryos through the IVF process. The Catholic Church clarified its position on embryo donation/adoption in 2008 in the Instruction from the Congregation of the Faith called Dignitas Personae. "The proposal that these embryos could be put at the disposal of infertile couples as a treatment for fertility is not ethically acceptable for the same reasons which make artificial heterologous procreation illicit as well as any form of surrogate motherhood; this practice would also lead to other problems of a medical, psychological and legal nature" [47]. This statement by the Magisterium removes donation/adoption as a viable option for Catholics. The only remaining option would be to allow these embryos to die with dignity and respect using the extraordinary/ordinary means distinction. To determine if thawing these embryos and allowing them to die naturally is ethical and to address the ambiguities and unresolved issues surrounding this controversy, the traditional ethical principle of the extraordinary/ordinary means distinction will be examined and applied to this situation. The history of the Catholic Church's position on the ordinary-extraordinary means distinction dates back to the 16th century Dominican moralists. There are, however, some who believe it may go back to Thomas Aquinas (1225-1274), Dominican Friar and Doctor of the Roman Catholic Church. Thomas' belief in the moral measure of all human activity is whether it leads to God, the final end. Thus, if something was "too difficult" or "too burdensome" what was implied was that it might make

loving God too difficult [48]. The general obligation to preserve life and the possible limits to that obligation are also influenced by Thomas' concept of God's dominion over the gift of human life, responsible stewardship and the positive and negative precepts derived from these [49]. Thomas' influence is clearly present, but it is the three Dominican moralists–Francisco De Vitoria, Domingo Soto and Domingo Banez-who articulated the foundation of the ordinary-extraordinary means distinction. De Vitoria (1486-1546) examined the limits of treatment in regards to nourishment and medicinal drugs. In his seminal work Relectiones Theologicae, he states:

> "If a sick man can take food or nourishment with a certain hope of life, he is required to take food as he would be required to give it to one who is sick. However, if the depression of spirits is so severe and there is present grave consternation in the appetitive power so that only with the greatest effort and as though through torture can the sick man take food, this is to be reckoned as an impossibility and therefore, he is excused, at least from mortal sin" [50] [51].

De Victoria is not condoning suicide here. A healthy person may not starve him-herself because life is problematic. If the means are effective and not burdensome then the person is morally obligated to seek nourishment. However, if the person is so sick or depressed that eating may become a grave burden, then the person is not morally obliged to eat and does not commit a sin. The essential point here is that De Vitoria recognizes both psychological and physiological illness and his notion of grave burden includes both. In regards to medicinal drugs, he argues that they are not per se obligatory. The obligation to use them rested on the degree of efficacy. One is not obliged to sacrifice one's whole means of subsistence, nor one's general lifestyle, nor one's homeland in order to acquire a cure or obtain optimum health [51]. It appears that De Vitoria adopted the 16th century's version of the "Reasonable Person" criteria. "To fulfill one's positive obligation to sustain life, it is sufficient to perform 'that by which regularly a man can live'" [51]. The moral components that appear operative here are not natural as opposed to artificial means, but those means that offer a reasonable hope of benefit in regard to cure and return to health. Excessive burdens in terms of financial costs or inconvenience of lifestyle are measured by "the semi-objective standard of the common person regularly considered," or what we refer to as the "reasonable person standard" [51]. If the means used to prolong life were ineffective, if the effect was doubtful, or if it involves a grave burden for the person in question, this means need not be morally obligatory.

Prior to the development of modern anesthesia, surgical procedures, especially amputations, were quite painful. Domingo Soto (1494-1560) reasoned that surgery such as amputation of a limb, because of the excessive pain, ought to be considered categorically optional. He argued that such torture was beyond the limits that the "common man" ought to be obliged to suffer for the sake of one's bodily health. Such surgery can make a beneficial surgery "morally impossible" to bear [51] [52]. Besides the question of pain, Soto also recognizes the role that emotions of fear and repugnance could play [53]. Soto incorporates the dimension of optional versus obligatory, adding if a procedure or treatment was too painful or burdensome, it would be morally optional.

In 1595, Domingo Bañez (1528-1604) was the first to articulate the terms "ordinary" and "extraordinary" as they regard obligatory and non-obligatory means of preserving life. He argued that if preserving life was reasonable it was obligatory but insisted that one is "not bound to extraordinary means but to common food and clothing, to common medicines, to certain common and ordinary pain; not, however, to certain extraordinary and horrible pain, nor to expenses which are extraordinary in proportion to the status of this man" [54]. One determined if a treatment or medical procedure was ordinary or extraordinary according to whether it was proportionate to one's condition or state in life. "Thus, if something were very costly or burdensome or if it did not offer substantial benefit to the patient, there was no moral obligation to use it. This standard applied to even life-saving measures" [55]. The Jesuit moralist Juan Cardinal De Lugo (1583-1660) confirms Bañez's position when he wrote, "…he is not held to the extraordinary and difficult means . . . the 'bonum' of his life is not of such great moment, however, that its conservation must be effected with extraordinary diligence. . ." [56]. De Lugo's position, like that of the Dominican moralists, followed the tradition of the Church that states human life is a good but not an absolute good. As a relative good, one's duty to preserve it is a limited duty. While a person has freedom over his or her life, one is never permitted to directly take one's life. The issue becomes to what extent is one obligated to preserve

one's life.

The traditional understanding of ordinary-extraordinary means remained basically unchallenged until the mid-1900s with the advent of advances in medicine and technology. How to apply the early distinction of ordinary-extraordinary means to issues like oxygen and feeding tubes, especially with permanently unconscious patients became hotly debated as early as the 1950s. Jesuit moralist Gerald Kelly was one of the first to examine this issue critically. He defined ordinary means of preserving life as "all medicines, treatments, and operations, which offer a reasonable hope of benefit for the patient, and which can be obtained and used without excessive expense, pain, or other inconvenience." Extraordinary means would be "all medicines, treatments, and operations, which cannot be obtained or used without excessive expense, pain, or other inconvenience, or which, if used, would not offer a reasonable hope of benefit" [57]. The distinctive element of Kelly's interpretation is that it is a patient-centered, quality-of-life approach which is consistent with how the 16th-century-Dominican moralists viewed this distinction. Kelly concludes that no person is morally obligated to use any means, and this would include natural or artificial means, that does not offer a reasonable hope of ameliorating the patient's condition. To clarify this distinction, Kelly was asked if oxygen and intravenous feeding must be used to extend the life of a patient in a terminal coma. He replies: "I see no reason why even the most delicate professional standard should call for their [oxygen and intravenous for a patient in a terminal coma] use. In fact, it seems to me that, apart from very special circumstances, the artificial means not only need not but should not be used, once the coma is reasonably diagnosed as terminal. Their use creates expense and nervous strain without conferring any real benefit" [57].

Many believe that the most authoritative historical study on this topic was done by Daniel Cronin (who later became Archbishop of Hartford) in his 1958 doctoral dissertation at the Gregorian University in Rome entitled, "The Moral Law in Regard to the Ordinary and Extraordinary Means of Preserving Life." After a review of over 50 moral theologians from Aquinas to those writing in the early 1950's Cronin concludes that the Church's teaching is consistent in its view: "Even natural means, such as taking of food and drink, can become optional if taking them requires great effort or if the hope of beneficial results (spes salutis) is not present." For a patient whose condition is incurable, he writes, "even ordinary means, according to the general norm, have become extraordinary [morally dispensable] for the patient [so] the wishes of the patient, expressed or reasonably interpreted, must be obeyed" [51] [58]. The importance of Cronin's position is that no means—even food and water—can ever be classified as absolutely obligatory regardless of the patient's condition. However, some moralists disputed this fact and claimed that food and water were absolutely ordinary and even tried to say that was what the tradition taught.

On November 24, 1957, in a talk delivered to the International Congress of Anesthesiologists, Pope Pius XII gave papal approbation to the ordinary-extraordinary means tradition that dates back to De Vitoria. Natural reason and Christian morals say that man (and whoever is entrusted with taking care of his fellow man) has the right and the duty in case of serious illness to take the necessary treatment for the preservation of life and health . . . But normally one is held to use only ordinary means—according to circumstances of persons, places, times and culture—that is to say, means that do not involve grave burden for oneself or another. A more strict obligation would be too burdensome for most men and would render the attainment of the higher, more important good too difficult. Life, health, and all temporal activities are in fact subordinated to spiritual ends. On the other hand, one is not forbidden to take more than the strictly necessary steps to preserve life and health, as long as he does not fail in some more serious duty [59].

Pius XII upholds the traditional ordinary-extraordinary means distinction that "involves patient-centered judgments about the quality of life, which must take into account the usefulness of the treatment, one's understanding about death and dying, and the repugnance one may have toward one's life after subjection to a particular medical treatment" [53]. It is also important to note that Pius XII emphasized the importance of viewing the person holistically. In an address given to the International Union Against Cancer, in 1956, Pius XII counseled that "before anything else, the doctor should consider the whole man, in the unity of his person, that is to say, not merely his physical condition but his psychological state as well as his spiritual and moral ideals and his place in history" [60]. This statement reinforces the traditional understanding of not treating the physiological aspect of the body separate from the person. Benefits of a treatment can only be determined within the context of a person's life [53]. To preserve life at all cost is to risk idolatry and thus would lead a person away from the higher spiritual good which is eternal life. A contemporary

understanding of the ordinary-extraordinary means distinction was given in the 1980 Congregation for the Doctrine of the Faiths' Declaration on Euthanasia. The Declaration follows the tradition on the ordinary-extraordinary means distinction since the 16th century, which is based on the effect of the treatment on the patient or those responsible for the care of the patient. The Declaration reminds us of the duty one has to care for one's own life and to seek such care for others. But there are limits to this obligation. One needs to judge the means used by "studying the type of treatment to be used, its degree of complexity or risk, its cost and the possibilities of using it, and comparing these elements with the result that can be expected, taking into account the state of the sick person and his or her physical and moral resources" [61]. The Declaration goes on to give four examples: patients are permitted to use experimental, advanced medical techniques, which may be a service to humanity; patients may interrupt treatments if they fall short of expectations; the refusal of a technique that is in use and carries a risk or is burdensome is not equivalent to suicide; finally, when death is imminent in spite of the means used, it is permitted in conscience to make the decision to refuse forms of treatment that would only secure a precarious and burdensome prolongation of life, so long as the normal care due to the sick person in similar cases is not interrupted [61]. Finally, the Congregation for the Doctrine of the Faith reflects the traditional teaching when it writes: "Life is a gift from God, and on the other hand death is unavoidable; it is necessary, therefore, that we, without in any way hastening the hour of death, should be able to accept it with full responsibility and dignity" [61]. The only real change is that the document realizes that the terms ordinary and extraordinary are imprecise as terms in regards to the rapid advancement of medicine and technology. More precise terms would be proportionate and disproportionate [61].

The historical review of the tradition shows a clear distinction between extraordinary and ordinary means that involves patient-centered judgments about the quality of life, which must take into account the usefulness of the treatment, one's understanding about death and dying, and the repugnance one may have toward one's life after subjection to a particular medical treatment [53]. The ethical issue concerning frozen embryos focuses on the foregoing of artificial life support from them, which would allow the embryos to die naturally. Some might argue that this is a form of euthanasia. Pope John Paul II in Evangelium Vitae states: "Euthanasia's terms of reference, therefore, are to be found in the intention of the will and in the methods used" [62] intention here is not to end the life of the embryo but to forego a burdensome treatment and allow the embryo to die naturally with dignity and respect. The Pope himself states clearly that euthanasia must be distinguished from the decision to forego what he refers to as "aggressive medical treatment". Medical procedures which no longer correspond to the real situation of the patient, either because they are by now disproportionate to any expected results or because they impose an excessive burden on the patient and his family [62]. If the intentionality is to forgo a non-beneficial treatment that the surrogate believes is disproportionate and not in the embryo's best interest, then the intentionality is to allow the person to die rather than not to terminate the person directly. These embryos will not be abandoned or discarded. Instead they will be cared for lovingly during the dying process and treated with the utmost dignity and respect.

The benefit of a medical procedure or treatment was traditionally viewed as a prudential judgment of the patient or surrogate on how a particular treatment or procedure would impact on the life of the patient. Benefits and burdens were never judged abstractly. "Not only the means (proposed intervention) but the ends toward which the intervention is aimed are important in moral analysis" [63]. The fact that a particular means was able to sustain a human life did not make such a means beneficial to the person. Traditional moralists did not restrict benefits merely to sustaining life, but included broader, more holistic considerations. Improvements in one's condition, relief of pain and suffering, maximization of comfort, restoration of health, among others all were considered beneficial. For DeVitoria and other traditional moralists, the mere preservation of life and vital physiological functions was not sufficient in itself to oblige someone to use a certain means.

The traditional understanding of ordinary-extraordinary means was based on treating the whole person, not one part of the person. Just because a treatment could prolong a life did not mean that a particular treatment was a benefit. Benefits must be considered worthwhile both in quality and duration. In the Catholic moral tradition, a medical treatment was beneficial if it restored a patient to a relative state of health. The frozen embryos will not be implanted into the womb of the biological mother. The options would be to stay frozen in a state of "permanent suspended animation," be used for stem cell research, be used for other forms of experimentation, or be placed for donation/adoption. The

Magisterium of the Catholic Church has rejected all of these options as ethically acceptable. To allow these embryos to stay frozen indefinitely violates the basic dignity and respect of the person. Therefore, the only viable option for these frozen embryos would be to stop the process of cryopreservation and allow them to die naturally with dignity and respect. One could equate the process of cryopreservation to maintain the life of the embryo to the use of a mechanical ventilator to maintain the life of a terminal patient. To continue to keep the embryos alive through cryopreservation is a form of extraordinary means that is disproportionate and offers no reasonable hope of benefit for the embryo. Failure to receive a meaningful benefit from a treatment makes said treatment not morally obligatory. Allowing a person to die by foregoing aggressive, non-beneficial treatments is not only morally permissible, it is also treating the person with dignity and respect. Therefore, it is morally and ethically acceptable to allow these embryos to die naturally with dignity and respect under the principle of the extraordinary and ordinary means distinction. However, it is also imperative that safeguards be put in place that would eliminate creating more "spare" embryos in the future.

CONCLUSION/SUGGESTIONS:

The Dobbs v. Jackson ruling has brought topics surrounding reproductive health to the forefront of legal, ethical, and medical discourse. As IVF becomes a more common ART procedure, the need for thoughtful legislation is highlighted. The current lack of consistent regulation for embryo disposition is arguably the main factor causing embryos to be left in indefinite storage. Lawmakers or fertility clinics must establish ways to help a patient reach a disposition decision before an IVF cycle, or mandate that patients decide before being given the option of long-term storage. If personhood of these spare embryos is to be maintained, then allowing them to thaw out is an ethical way of removing them from their perpetual life support. Keeping the embryos stored with no intention for future use is not only a needlessly expensive practice, but morally questionable as well. As the United States navigates an ever-changing legal landscape concerning reproductive rights, the need for an objective look at the implications of ART and its procedures are crucial. At minimum, awareness should be raised about the embryos left in indefinite storage, encouraging discourse for this very nuanced subject.

References

1. 1 in 6 people globally affected by infertility: WHO. (2023). Neurosciences (Riyadh, Saudi Arabia), 28(3), 208–209.

2. Fact Sheet: In Vitro (IVF) Use Across the United States. (2024, March 13). HHS.gov. https://www.hhs.gov/about/news/2024/03/13/fact-sheet-in-vitro-fertilization-ivf-use-across-united-states.html

3. Gracia, C. R., Gracia, J. J., & Chen, S. (2010). Ethical dilemmas in oncofertility: an exploration of three clinical scenarios. Cancer treatment and research, 156, 195–208. https://doi.org/10.1007/978-1-4419-6518-9_15

4. Nachtigall, R. D., Becker, G., Friese, C., Butler, A., & MacDougall, K. (2005). Parents' conceptualization of their frozen embryos complicates the disposition decision. Fertility and sterility, 84(2), 431–434. https://doi.org/10.1016/j.fertnstert.2005.01.134

5. Nachtigall, R. D., Mac Dougall, K., Harrington, J., Duff, J., Lee, M., & Becker, G. (2009). How couples who have undergone in vitro fertilization decide what to do with surplus frozen embryos. Fertility and sterility, 92(6), 2094–2096. https://doi.org/10.1016/j.fertnstert.2009.06.027

6. Lyerly, A. D., Nakagawa, S., & Kuppermann, M. (2011). Decisional conflict and the disposition of frozen embryos: implications for informed consent. Human reproduction (Oxford, England), 26(3), 646–654. https://doi.org/10.1093/humrep/deq368

7. Rinehart L. A. (2021). Storage, transport, and disposition of gametes and embryos: legal issues and practical considerations. Fertility and sterility, 115(2), 274–281. https://doi.org/10.1016/j.fertnstert.2020.11.025

8. Nash, E., & Guarnieri, I. (2023, September 5). Six Months Post-Roe, 24 US States Have Banned Abortion or are Likely to Do So: A Roundup. Guttmacher Institute. https://www.guttmacher.org/2023/01/six-months-post-roe-24-us-states-have-banned-abortion-or-are-likely-do-so-roundup

9. Roden G. J. (2010). Unborn children as constitutional persons. Issues in law & medicine, 25(3), 185–273.

10. State Legislation Tracker. (n.d.). Retrieved May 4, 2024, from https://www.guttmacher.org/state-legislation-tracker

11. The Associated Press. (2024, February 20). Alabama Supreme Court rules frozen embryos are "children" under State law. NPR. Retrieved from https://www.npr.org/2024/02/20/1232815486/alabama-supreme-court-frozen-embryos

12. Baker, L., Elliott, D., & Capelouto, S. (2024, March 6). Alabama governor signs IVF bill giving immunity to patients and providers. NPR. Retrieved from https://www.npr.org/2024/03/06/1235907160/alabama-lawmakers-pass-ivf-immunity-legislation

13. Dobbs v. Jackson Women's Health Organization. (2022). Retrieved from https://casetext.com/case/dobbs-v-jackson-womens-health-organization

14. Aspinwall, C., Bailey, B., & Yurkanin, A. (2022, September 1). They Lost Their Pregnancies. Then

Prosecutors Sent Them to Prison. The Marshall Project. Retrieved from https://www.themarshallproject.org/2022/09/01/they-lost-their-pregnancies-then-prosecutors-sent-them-to-prison#:~:text=More%20than%2050%20women%20have,published%20in%20partnership%20with%20The

15. Flaherty, A., & Kekatos, M. (2024, January 11). Grand jury declines to indict Ohio woman facing charges after she miscarried. ABC News. Retrieved from https://abcnews.go.com/Health/grand-jury-declines-indict-ohio-woman-facing-charges/story?id=106082483

16. Szekely, P. (2019, July 3). Alabama prosecutor drops charges against woman who lost fetus after being shot. Reuters. Retrieved from https://www.reuters.com/article/idUSKCN1TY2Q9/

17. Milford S. (2023). Relating to foetal persons: why women's Voices come first and last, but not alone in Abortion debates. Medicine, health care, and philosophy, 26(3), 293–300. https://doi.org/10.1007/s11019-023-10144-0

18. Crockin, S., Altman, A. B., & Rinehart, L. (2023). Post-Dobbs legal conundrums surrounding preimplantation in vitro fertilization embryo dispositions. Fertility and sterility, 119(1), 21–26. https://doi.org/10.1016/j.fertnstert.2022.10.033

19. Cohen, I. G., & Adashi, E. Y. (2016). Embryo Disposition Disputes: Controversies and Case Law. The Hastings Center report, 46(4), 13–19. https://doi.org/10.1002/hast.600

20. Pregnancy Justice. (2022). When Fetuses gain personhood: Understanding the impact on IVF, contraception, medical treatment, criminal law, child support, and beyond. Retrieved June 10, 2024, from https://search.issuelab.org/resource/when-fetuses-gain-personhood-understanding-the-impact-on-ivf-contraception-medical-treatment-criminal-law-child-support-and-beyond.html

21. Zhang, Mark, Chapman, Jennifer E., "Davis v. Davis (1992)". Embryo Project Encyclopedia (2013-10-17). ISSN: 1940-5030 https://hdl.handle.net/10776/6320

22. Crockin, S. L., & Gottschalk, K. C. (2018). Legal Issues in Gamete and Embryo Cryopreservation: An Overview. Seminars in reproductive medicine, 36(5), 299–310. https://doi.org/10.1055/s-0038-1676852

23. Teoh, P. J., & Maheshwari, A. (2014). Low-cost in vitro fertilization: current insights. International journal of women's health, 6, 817–827. https://doi.org/10.2147/IJWH.S51288

24. Ranji, Usha, et al. (2022, September 15). Coverage and Use of Fertility Services in the U.S. KFF. Retrieved from www.kff.org/womens-health-policy/issue-brief/coverage-and-use-of-fertility-services-in-the-u-s/.

25. Alikani, M., & Parmegiani, L. (2018). Human Reproductive Cell Cryopreservation, Storage, Handling, and Transport: Risks and Risk Management. Seminars in reproductive medicine, 36(5), 265–272. https://doi.org/10.1055/s-0038-1676849

26. Choe J, Shanks AL. In Vitro Fertilization. [Updated 2023 Sep 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562266/

27. Niederberger, C., Pellicer, A., Cohen, J., Gardner, D. K., Palermo, G. D., O'Neill, C. L., Chow, S., Rosenwaks, Z., Cobo, A., Swain, J. E., Schoolcraft, W. B., Frydman, R., Bishop, L. A., Aharon, D., Gordon, C., New, E., Decherney, A., Tan, S. L., Paulson, R. J., Goldfarb, J. M., … LaBarbera, A. R. (2018). Forty years of IVF. Fertility and sterility, 110(2), 185–324.e5. https://doi.org/10.1016/j.fertnstert.2018.06.005

28. Zhao, Y., Brezina, P., Hsu, C. C., Garcia, J., Brinsden, P. R., & Wallach, E. (2011). In vitro fertilization: four decades of reflections and promises. Biochimica et biophysica acta, 1810(9), 843–852. https://doi.org/10.1016/j.bbagen.2011.05.001

29. Shrestha, D., La, X., & Feng, H. L. (2015). Comparison of different stimulation protocols used in in vitro fertilization: a review. Annals of translational medicine, 3(10), 137. https://doi.org/10.3978/j.issn.2305-5839.2015.04.09

30. Doody K. J. (2021). Infertility Treatment Now and in the Future. Obstetrics and gynecology clinics of North America, 48(4), 801–812. https://doi.org/10.1016/j.ogc.2021.07.005

31. Debrock, S., Peeraer, K., Fernandez Gallardo, E., De Neubourg, D., Spiessens, C., & D'Hooghe, T. M. (2015). Vitrification of cleavage stage day 3 embryos results in higher live birth rates than conventional slow freezing: a RCT. Human reproduction (Oxford, England), 30(8), 1820–1830. https://doi.org/10.1093/humrep/dev134

32. Wong, K. M., Mastenbroek, S., & Repping, S. (2014). Cryopreservation of human embryos and its contribution to in vitro fertilization success rates. Fertility and sterility, 102(1), 19–26. https://doi.org/10.1016/j.fertnstert.2014.05.027

33. Rienzi, L., Gracia, C., Maggiulli, R., LaBarbera, A. R., Kaser, D. J., Ubaldi, F. M., Vanderpoel, S., & Racowsky, C. (2017). Oocyte, embryo and blastocyst cryopreservation in ART: systematic review and meta-analysis comparing slow-freezing versus vitrification to produce evidence for the development of global guidance. Human reproduction update, 23(2), 139–155. https://doi.org/10.1093/humupd/dmw038

34. Edgar, D. H., & Gook, D. A. (2012). A critical appraisal of cryopreservation (slow cooling versus vitrification) of human oocytes and embryos. Human reproduction update, 18(5), 536–554. https://doi.org/10.1093/humupd/dms016

35. Myhre, Reigstad & Storeng, Ritsa. (2019). Development of In Vitro Fertilization, a Very Important Part of Human Reproductive Medicine, in the Last 40 Years. International Journal of Women's Health and Wellness. 5. 10.23937/2474-1353/1510089.

36. Wang, R., Pan, W., Jin, L., Li, Y., Geng, Y., Gao, C., Chen, G., Wang, H., Ma, D., & Liao, S. (2019). Artificial intelligence in reproductive medicine. Reproduction (Cambridge, England), 158(4), R139–R154. https://doi.org/10.1530/REP-18-0523

37. Weng L. (2019). IVF-on-a-Chip: Recent Advances in Microfluidics Technology for In Vitro Fertilization. SLAS technology, 24(4), 373–385. https://doi.org/10.1177/2472630319851765

38. Thapa, S., Heo, Y.S. Microfluidic technology for in vitro fertilization (IVF). JMST Adv. 1, 1–11 (2019). https://doi.org/10.1007/s42791-019-0011-3

39. VerMilyea, M., Hall, J. M. M., Diakiw, S. M., Johnston, A., Nguyen, T., Perugini, D., Miller, A., Picou, A., Murphy, A. P., & Perugini, M. (2020). Development of an artificial intelligence-based assessment model for prediction of embryo viability using static images captured by optical light microscopy during IVF. Human reproduction (Oxford, England), 35(4), 770–784. https://doi.org/10.1093/humrep/deaa013

40. Saitou, M., & Hayashi, K. (2021). Mammalian in vitro gametogenesis. Science (New York, N.Y.), 374(6563), eaaz6830. https://doi.org/10.1126/science.aaz6830

41. Kass, L. (2002). Life, Liberty, & the Defense of Dignity: The Challenge for Bioethics. Encounter Books.

42. Moore, K. L., Persaud, T. V. N. (2008). The Developing Human: Clinically Oriented Embryology (8th ed.) Saunders.

43. Holy See. (1983). Charter of the rights of the family (No. 4). L'Osservatore Romano.

44. Congregation for the Doctrine of the Faith. (1987). Donum vitae: Instruction on respect for human life in its origin and on the dignity of procreation—Replies to certain questions of the day (1-29). http://www.priestsforlife.org/magisterium/donumvitae.htm

45. Brugger, E. C. (2008). The Principle of Fairness and the Problem of Abandoned Embryos. In Panel discussion at the Conference on Emerging Issues in Embryo Donation and Adoption, Washington, D.C. (1-6).

46. Lysaught, T. (2003). Embryo Adoption? Human Life Review, 1-4. http://findarticles.com/p/articles/mi_qa3798/is_200310/ai_n9297175/print

47. Congregation for the Doctrine of the Faith. (2008). Instruction Dignitas Personae on Certain Bioethical Questions (1-23, Section 2, #18).

48. Atkinson, G. (1981). Theological History of Catholic Teaching on Prolonging Life. In D. McCarthy & A. Moraczewski (Eds.), Moral responsibility in prolonging life decisions (xx-xx). Pope John Center.

49. Aquinas, T. (1966). Summa Theologica (A. Ross & P. G. Walsh, Eds.). Blackfriars edition. McGraw-Hill.

50. De Vitoria, F. (1957). Relectiones Theologicae (Relectio IX, de Temp., n. 12). Lugdini.

51. Sparks, R. (1988). To Treat or Not to Treat. Paulist Press.

52. Soto, D. (1568). De Justitia et Jure (Lib. 5, question 2, article 1).
53. Wildes, K. (1996). Ordinary and extraordinary means and the quality of life. Theological Studies, 57, 500-512.

54. Bañez, D. (1614-1615). Scholastica Commentaria in Partem Angelici Doctoris S. Thomae (Vol. IV, "Decisiones de Jure et Justitia," II, IIae, Question 65, Article 1).

55. Paris, J., & McCormick, R. (1987). The Catholic Tradition on the Use of Nutrition and Fluids. America, 156, 356-361.

56. De Lugo, J. (1642). Disputationum de Justitia et Jure (10, section 1, n. 9)

57. Kelly, G. (1950). The Duty of Using Artificial Means of Preserving Life. Theological Studies, 11, 203-220.

58. Cronin, D. (1958). The Moral Law in Regard to Ordinary and Extraordinary Means of Conserving Life. Gregorian University, Rome.

59. Pius XII. (1958). Prolongation of life. The Pope Speaks, 4, 395-396.

60. Pius XII. (1957). Cancer: A Medical and Social Problem. The Pope Speaks, 3, 48.

61. Congregation for the Doctrine of the Faith. (1980). Declaration on Euthanasia (Part 4). Origins, 10, 154-157.

62. John Paul II. (1995). Evangelium Vitae (No. 65). Origins, 24, 687-727.

63. Shannon, T., & Walter, J. (2004). Artificial Nutrition & Hydration: Assessing Papal Statement. National Catholic Reporter, 1-4. http://www.natcath.com/NCR_online/archives2/2004b/041604/041604i.php

Author Information

Jeffrey Hernandez, M.D., PL-2
Pediatrics Residency, St. Christopher's Hospital for Children
Philadelphia, PA

Peter Clark, S.J., Ph.D.
Director of Institute of Clinical Bioethics, Saint Joseph's University
Philadelphia, PA

Ally Borgia
Philadelphia College of Osteopathic Medicine
Philadelphia, PA

Artiom Butuc, Research Fellow
Institute of Clinical Bioethics, Saint Joseph's University
Philadelphia, PA

Jessica Haddad, Research Fellow
Institute of Clinical Bioethics, Saint Joseph's University
Philadelphia, PA

Samantha Lerner
Philadelphia College of Osteopathic Medicine
Philadelphia, PA

Davina Odeh, Research Fellow
Institute of Clinical Bioethics, Saint Joseph's University
Philadelphia, PA

Maanav Patel
Philadelphia College of Osteopathic Medicine
Philadelphia, PA