

FROZEN EMBRYO ADOPTION

LA ADOPCIÓN DE EMBRIONES CONGELADOS

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Fecha de recepción y aceptación: 17 de abril de 2016 y 28 de mayo de 2016

Abstract: The existence of a large number of frozen human embryos is a major medical and ethical concern. There are four possible solutions for these embryos: a) leave them frozen indefinitely; b) thaw them so that they die; c) use them for biomedical research or d) donate them to an infertile couple who wish to have children.

Donation for procreation appears to be the best of these solutions. Nevertheless, it too raises ethical issues that should be assessed.

First, though, the current situation of frozen embryos should be reviewed, as we have done in this paper, setting ourselves various objectives: 1. To assess how many frozen embryos currently exist worldwide, or in some particular countries. 2. To look at how long frozen embryos can maintain viability for use, which seemingly could exceed 10 years. 3. To evaluate the efficacy of the transfer technique, which at present varies between approximately 45% and 80%. 4. To define the meaning of the word “adoption”, since it can be used in different senses; here it is used to mean the donation of cryopreserved embryos to be transferred to a woman who wishes to enlarge her family, with the

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consent of the biological parents. 5. To review some historical data on the freezing of human embryos, the countries that offer this practice, and some technical aspects of the procedure. 6. To also examine the legal regulations regarding frozen human embryo donation in Spain and other countries (mainly European), evaluating the economic costs of this process, and identifying whether there are agencies dedicated to this practice.

In conclusion, we can say that, at the present time, there is a large number of frozen human embryos. Given the incompatibility of this situation with their dignity, it is therefore a medical, ethical and social necessity to seek a solution to this dilemma.

Keywords: frozen human embryos, frozen human embryo adoption, medical assessment, ethical assessment and social assessment.

Resumen: La existencia de un gran número de embriones humanos congelados es un importante problema médico y ético. A dichos embriones se les pueden dar cuatro soluciones: a) dejarlos congelados indefinidamente; b) descongelarlos para que mueran; c) utilizarlos para investigaciones biomédicas, o d) donarlos a una pareja infértil que desee tener un hijo. De estas soluciones la donación para procreación parece la más acertada. Sin embargo, esta también plantea problemas éticos que conviene evaluar.

Pero previamente a ello parece de interés revisar la situación actual de los embriones congelados, cosa que hacemos en este trabajo, planteándonos diversos objetivos: 1. Valorar cuántos embriones congelados hay actualmente en el mundo o en algunos países concretos. 2. Ver cuánto tiempo pueden mantener la viabilidad para su uso los embriones congelados, tiempo que al parecer puede superar los 10 años. 3. Evaluar la eficacia de la técnica de transferencia, que en el momento actual oscila entre el 45 y el 80 % aproximadamente. 4. Definir el significado de la palabra *adopción*, pues esta puede utilizarse en distintos sentidos; aquí se utiliza como la donación de embriones crioconservados para ser transferidos a una mujer que desea aumentar su familia, con el consentimiento de los padres biológicos. 5. También es de interés repasar algunos datos históricos sobre la congelación de embriones humanos, los países que ofrecen esta práctica y algunos aspectos técnicos de esta. 6. Igualmente es necesario conocer la regulación legal de la donación de embriones humanos congelados en España y en otros países, fundamentalmente europeos, así como evaluar los costes económicos de esta práctica y conocer si existen agencias que se dediquen a ello.

En conclusión, se puede afirmar que en el momento actual hay un gran número de embriones humanos congelados, situación ésta que es incompatible con su propia dignidad, por lo que parece una necesidad médica, ética y social buscar una solución para dicho problema.

Palabras clave: embriones humanos congelados, adopción de embriones humanos congelados, valoración médica, valoración ética y valoración social.



INTRODUCTION

Since Louise Brown, the first child to be conceived through in-vitro fertilisation (IVF), was born, around five million children have been conceived through IVF or intracytoplasmic sperm injection (ICSI) (1), (2), which clearly translates into great social acceptance of assisted reproduction techniques.

The production of frozen embryos in IVF is a direct consequence of creating more embryos than can be transferred, making it necessary to freeze those not used. This is because the quest for improved efficacy of the technique takes precedence over respect for the lives of these surplus embryos. In fact, it is known that IVF has low efficacy, as the pregnancy rate per treatment cycle does not usually exceed 30% in 2006 (3), percentages that remain practically equal in the following years: 2007, 29,10% (4); 2008, 28,5% (5); 2009, 28,9% (6) and 2010, last year for which data have been published, 29,10% (7).

Accordingly, in order to avoid new ovarian stimulation cycles (which among other things entail a risk for the woman (3)), more embryos than necessary are produced for the first transfer cycle, meaning that some are left over. These are frozen and can then be used later after thawing to begin further attempts to achieve the desired pregnancy. This is considered an advantage, since avoiding another stimulation cycle could be safer and cheaper to the women.

“This practice means that the number of frozen embryos is increasing daily, so a medically correct and ethically acceptable solution must be found for them”.

To solve this problem, the definitive solution would be to not produce more embryos than can be transferred, but this would reduce the effectiveness of the technique. This of course would be an undesirable consequence for those who run assisted reproduction clinics, as the efficacy in achieving new pregnancies is the main reason for attracting new clients. Ethical utilitarianism prevails in assisted procreation.

Consequently, not only is the number of frozen embryos not diminishing; it is rising.

In this paper, we have reviewed various technical and medical aspects related to the frozen human embryo adoption to determine the current status of the problem, covering historical, legal, social and medical aspects.

HOW MANY FROZEN EMBRYOS ARE THERE CURRENTLY?

Although there are no reliable data on the number of embryos stored frozen worldwide, there are approximate data for some countries. In the United States, in 2003, there were around 400,000 frozen embryos (more specifically 396,526) (8) according to



a survey sponsored by the RAND corporation, which collected data from 430 assisted reproduction clinics, 79% of which replied (8). Given that the number in the U.S. is increasing annually by 19,000 (9), it is safe to say that in 2013 there could be around 700,000 embryos in their freezers. Moreover, it is also known that only 4% of cryopreserved embryos are available for donation (10), and that only 2% of frozen embryos are used for infertility treatments, which means that the vast majority of them will remain in a frozen state (11).

In the United Kingdom, the exact number of frozen embryos cannot be determined either, although it is known that around 45,000 embryos are frozen and stored every year (12), meaning that around half a million will have been frozen in the last 10 years.

In Italy, however, there are very few frozen embryos: only 1,863 in 2008 and 7,737 in 2009 (13).

In Spain, there may be more than 200,000 frozen embryos, but there are no specific data on those that could be stored in the 180 to 200 Spanish assisted reproduction clinics either.

However, a recent study by Nadal Pereña and del Castillo (14), which included data from 104 Spanish assisted reproduction clinics (24 public and 80 private; 66.62% of all clinics in Spain), found that, in December 2010, there were 145,261 frozen embryos. The authors therefore assumed that if the 33% of centres that did not provide figures have an equivalent number of frozen embryos, it could be reasonably estimated that in December 2012, this figure could rise to 217,892, i.e. 4.6 embryos per 1000 inhabitants, a big number compared to the 1.6 per 1000 inhabitants in the United States.

HOW LONG CAN EMBRYOS REMAIN FROZEN WITHOUT LOSING THEIR VITALITY?

Another question that arises in relation to frozen embryos, in addition to how many are used for reproductive purposes, is their survival in a frozen state in conditions suitable for subsequent transfer. Although this has not been completely determined, the topic has been reviewed, and according to some authors, cryopreservation did not have a significant effect on postthaw survival for IVF or oocyte donation cycles, or for embryos frozen at the pronuclear or cleavage stages. There was no significant impact of the duration of storage on clinical pregnancy, miscarriage, implantation, or live birth rate, whether from IVF or oocyte donation cycles (15). The study reports that there are data on embryos that were thawed out after having been cryopreserved for 9.2 years and were then able to be used for reproductive purposes, although in their opinion, at that time there were no objective data to conclude that embryos could be used after 10 years of



storage (15). Nevertheless, other authors mention the possibility of using embryos after 12 or 13 years of freezing (16) (17), and even make reference to an embryo that had been frozen for 13.5 years and from which a live baby had been born (18).

Limited studies of obstetric outcome, as well as further follow-up of the born children, indicate that cryopreservation of embryos is a safe procedure (19); nevertheless, long-term follow-up of the born children is still warranted (20), (21), (22).

EMBRYO BANKS

In order to improve efficiency in the use of frozen embryos for reproductive purposes, the creation of embryo banks from human gametes has been proposed, which has opened the possibility of promoting a potential embryo industry for purely procreative purposes (23). According to an article published in the Los Angeles Times (24), a Californian clinic wants to substantially cut the costs of storage and use of frozen embryos, by creating a batch of embryos from one egg donor and one sperm donor, then dividing it up so that it can be used for several patients.

In Spain, the Instituto Marqués in Barcelona has set up an embryo bank using embryos donated by their biological parents, although only those from donors under 35 years old are used (25).

PURPOSE OF FROZEN EMBRYOS

Four possible last uses have been suggested nowadays for frozen embryos: a) transferring them to a woman, its biological mother or another; b) using them for research; c) leaving them frozen indefinitely and d) thawing them and subsequently allowing them to perish (26).

In view of these possibilities, the Ethics Committee of the American Society for Reproductive Medicine (ASRM) (27) has proposed the establishment of specific standards of conduct in relation to the issue of frozen embryos, specifying in the first place that their condition of abandoned embryos should be ensured, which requires at least five years to have passed since the clinic's last contact with the individual or couple, and provided diligent efforts have been made to contact them. These legal provisions may, of course, vary from country to country. If these conditions are met, it is thought that abandoned embryos would only account for between 5% and 7% of those frozen.



EFFICACY OF THE TECHNIQUE

The pregnancy rate per embryo transfer ranges between 45.7% and 77% (28). In relation to this, Keenan *et al.* (29) evaluated data from ten series, concluding that the pregnancy rate is 44.7% and live birth rate is 35.5%. A recent review by the Center for Disease Control and Prevention in the United States estimates that this figure is around 35% (30).

At the European Society of Human Reproduction and Embryology (ESHRE) Congress held in Istanbul in 2012 (31), Checa presented a meta-analysis in which 633 IVF cycles from 64 studies were evaluated. It was found that the pregnancy rate for fresh embryos was 38%, compared to 50% when embryos that had been frozen for at least one month were used. It also found that the pregnancy rate after thawing embryos was higher than that obtained using fresh embryos, which has been confirmed by some authors (32), (33), (34), but not others (35), (36). However, a systematic review in 2012 (37), showed that singleton pregnancies after thawing and warming showed better results than with fresh embryos.

On the other hand, it is well established that improved embryo quality correlates with better results (38), (39), (40), (41), (42), (43), (44).

DEFINITION OF EMBRYO ADOPTION

Embryo donation or adoption is the compassionate gifting of cryopreserved embryos for transfer, with the consent of the biological parents, to an infertile woman (23). However, this definition can be extended, as they can also be transferred to fertile women, even those with children, in order to save the lives of those embryos.

The 2006 Spanish Law on Assisted Reproduction Techniques defines embryo donation, for the authorised purposes, as a free, formal and confidential contract agreed between the donor and an authorised medical centre. It must be formalised in writing after the donor has been informed of the purposes and consequences of the act, such as adoption by other couples; it must never be for profit and is always anonymous (45).

However, in other contexts, donation and adoption can have different meanings. Thus, according to the U.S. Embryo Adoption Awareness Center, (46), donation is used in the sense of “giving a gift” and in some way means an emotional separation for the donor couple. Adoption is a term that, both legally and socially, transfers parental rights to another couple, as occurs in post-natal adoption. Adoption is the voluntary acceptance of a child of other parents to eventually consider it as one’s own child.



For other people, the difference between adoption and donation is merely a legal concept. In donation, the embryos come from couples who have expressly relinquished them in writing to other couples, while in adoption, a use has not been determined for embryos that remain indefinitely in the custody of the Reproductive Centre. These are abandoned embryos whose fate is decided by the centre's medical team (47).

From a legal point of view, it has also been suggested that prenatal adoption could be assigned similar regulations to post-natal adoption, so that both forms have the same intent: to offer a child the prospect of a better life; prenatal adoption also includes the frozen embryo's vital need for adoption, as its only alternative is death.

Another aspect widely debated in bioethics literature in relation to embryo adoption is the so-called "conditional donation", which is where the embryo recipients are previously screened by the donor, in accordance with certain characteristics.

For some authors, this type of adoption poses objective ethical problems, particularly that potential adoptive parents could be discriminated against on the grounds of religion, race or sexual orientation. They believe, therefore, that conditional donation could result in unfair discrimination against potential adopters.

For the Ethics and Law Advisory Committee (ELAC), however, in a statement in June 2011 (48), "conditional donation" (49) does not present any ethical difficulties. In contrast, they consider that it should be promoted, although regulated by the competent health authority; in any case, contrary to what one might think, they say it is rare for donors to put conditions for donation.

Likewise, the ASRM (50) is in favour of "conditional donation", stating that the main argument for allowing donors to place conditions for the donation is that they are independent and therefore have the right to specify what type of person or couple may be suitable to receive their embryonic child, although it also mentions that it could have negative ethical aspects by being able to foster racist or homophobic attitudes.

HISTORICAL DATA

From a historical point of view, it is known that the first data on embryo donation dates back to the mid-eighties, as this was when the first frozen embryo donations were made (51) (52), resulting in pregnancies. January 1984 saw the birth of the first child to be born worldwide through embryo donation, in Long Beach, California (53) (54). The news was very shocking socially, and provoked considerable ethical debate.

In 1994, embryo donation was approved by the U.S. Bioethics Commission, but it would not be until five years later, in 1999, when this authorisation came into effect, despite the fact that there were no apparent technical difficulties to explain the delay (55).



In 1997, also in the United States, the first programmed embryo donation by a private organisation took place through the Snowflakes programme, sponsored by Nightlight Christian Adoptions (55).

In Australia, embryo donation has been ongoing for more than two decades (56).

In New Zealand, it was approved in 2005 (57).

In Spain, the Instituto Marqués in Barcelona was the first to offer embryo adoption in 2004 (47), to solve the problem that had arisen with the accumulation of thousands of frozen embryos in the clinic.

The first child born in Spain after embryo adoption was in the aforementioned Instituto Marqués on 2 September 2005.

Five months later, a second child was born in Gerona to a 40-year-old woman, from an embryo that had been frozen for 13 years (58), (59).

In 2004, the Centro Médico Cima, with the support of the Instituto Marqués, offered a total of 728 surplus embryos to people who wanted to have a child. Two hundred and twenty eight were used for fertilization and 68 pregnancies were achieved, 12 of which were twin pregnancies (60).

COUNTRIES THAT OFFER EMBRYO DONATION

There are no reliable data on the number of countries that offer embryo donation. However, it is estimated that among all the countries worldwide that offer infertility treatments, only 41 have embryo donation programmes, while this practice is banned in a further 14 (Germany, China, Denmark, Slovenia, Israel, Italy, Latvia, Norway, Sweden, Switzerland, Taiwan, Tunisia and Turkey) (61).

TECHNICAL ASPECTS

Although it may vary slightly between clinics, treatment for embryo adoption is essentially simple and painless. The woman who is to receive the embryo is first prepared using hormone skin patches and vaginal pessaries, although there are also other forms for administering the medication. After a few days, the embryos are thawed and transferred. The procedure does not require hospital admission; the patient must simply rest at home. Fourteen days later, a pregnancy test is carried out and if positive, the new pregnancy will require the same care as any other (62).

However, one question that arises is to determine whether the quality of the embryos influences the efficiency of the technique. Although not well determined, it is



known is that many healthy children have been born from supposedly poor quality embryos (63).

CHILDREN BORN AFTER PRENATAL ADOPTION

The number of children born as a result of this practice does not appear to be very high. Nightlight stated that in 2010, 480 donor families had been matched with 378 adoptive families. There were around 3075 frozen donor embryos. That same year, they reported that 242 children had already been born and that 19 adoptive families were currently expecting a further 24 children (64). According to Collard and Kashmeri, (55), fewer than 200 embryo adoption cycles had been carried out in the United States up to 2008, and up to 2010, the last year in which there are reliable data, fewer than 1000 embryos had been donated (23). In June 2013, more than 325 children had been born through the Snowflakes programme (65), although it can be assumed that the number born through frozen embryo donation will rise, as it is increasing by 25% annually (66).

In England, 1218 children were born through embryo donation between 1992 and 2009, while in 2010, 269 women chose this option (53).

In Spain, according to data from the Reproductive Medicine Department at Instituto Dexeus in Barcelona, 51 embryo donation cycles were carried out during the period 2006-2010, a very small figure if we compare it with egg donation, which in the same time period was 1734. One hundred and eighty-three transfers were performed between 1986 and 2010 (67).

At the Instituto Marqués in Barcelona, there were 58 births in 2006 as a result of frozen embryo transfer, 60 in 2007, 122 in 2008 and 146 in 2009, i.e. the clinic recorded 386 births up to 2009. As 12% were twins, the number of children born up to 2009 was 432, with a further 65 in 2010 (68). According to the Institute's director, Dr. López Teijón, 500 children had been born up to 2012, reaching 501 in 2013 (69).

LEGAL REGULATION OF FROZEN EMBRYO ADOPTION IN SPAIN

Law 35/1988 was the first to regulate gamete and "pre-embryo" donation. This law stipulates that donors must meet a series of conditions: they must be adults; males must be no older than 50 and females no older than 35; in both cases, they must have full capacity to act; they must be in good physical and mental health; they must have no family history of malformations linked to chromosomes, genes or metabolic disorders and



one or both members of the couple must not have produced six or more descendants. Furthermore, the assisted reproduction clinic has a responsibility to check the donor's identity and ensure that this premise is fulfilled.

After the law of 1998, Spanish law 14/2006 of 26 May (45), on Human Assisted Reproduction Techniques, determines the different possible uses for cryopreserved pre-embryos as well as cryopreserved semen, oocytes and ovarian tissue (as applicable), as mentioned above: a) use by the woman herself or her partner; b) donation for reproductive purposes; c) donation for research and d) termination of their conservation with no further use. In the case of cryopreserved pre-embryos and oocytes, the latter option will only be applicable once the maximum storage period established in this Act has expired, without any of the options listed in the previous sections having been chosen.

It also establishes that the use of pre-embryos (or cryopreserved semen, oocytes or ovarian tissue as applicable) for any of the purposes cited will require the appropriate duly accredited informed consent. In the case of pre-embryos, consent must be given by the woman or, if married to a man, by the husband as well, prior to the creation of the pre-embryos.

It also stipulates that consent to donate cryopreserved "pre-embryos" or gametes for any of the aforementioned uses can be amended at any time prior to its application.

Likewise, in the case of pre-embryos, the biological mother or couple will be asked to renew or amend the previously signed consent form at least every two years. If the biological mother or couples' signature of the appropriate consent form cannot be obtained for two consecutive renewals, and it can be reliably proven that all actions taken to obtain this renewal were unsuccessful, pre-embryos cryopreserved in the centre shall be at the clinic's disposal, and may be used for any of the aforementioned purposes at their discretion, while maintaining the established confidentiality and anonymity requirements and its gratuitous and non-profit nature.

Prior to giving consent, the biological mother or couple, as applicable, must be informed of the provisions in the preceding paragraphs of this section.

In summary, in relation to frozen embryos, law 14/2006, of 26 May, on Human Assisted Reproduction Techniques establishes that embryos left over from IVF may be stored for later transfer to the patient herself, donated for research or relinquished to other couples. This law also stipulates that, if the donor couple do not respond after several requests, after four years of silence the frozen embryos will remain in the custody of the centre, which may now transfer them to another patient.

Article 33.1 of Spanish law 14/2007 on Medical Research states: "The creation of human pre-embryos and embryos solely for research purposes is prohibited". Therefore, in Spain, the main source of frozen embryos is those left over from IVF, as according to article 28 of the above Law "Human embryos that have lost their capacity for biological



development, as well as dead human embryos or fetuses, may be donated for biomedical research or other diagnostic, therapeutic, pharmacological or surgical purposes". Frozen embryo adoption can undoubtedly be included among these uses.

LEGAL REGULATION OF FROZEN EMBRYO ADOPTION IN EUROPE

With respect to the donation and cryopreservation of embryos, only Norwegian law expressly prohibits donation, allowing this storage technique for a period not greater than 12 months in order for them to be transferred.

Germany and Sweden have not taken a position, although the latter has rejected embryo donation in a government report.

Britain and France expressly accept embryo donation and freezing, although their laws provide that the period during which embryos may be stored frozen must not exceed 5 years. Although Denmark does not state it by law, the Danish Ethics Committee accepts both procedures in their recommendations (60).

FINANCIAL ASPECTS

Naturally, the economic costs vary considerably between countries, although the price of frozen embryo adoption is generally lower than IVF processes and of course, post-natal adoption (70). In the United States, frozen embryo adoption is the cheapest form of adoption (70), as the cost for the adopters ranges between 6,000 and 15,000 U.S. dollars, divided as follows: between 2,500 and 8,000 dollars for the adoption agency; between 1,000 and 2,500 dollars for the adoptive family home study and between 2,500 and 4,000 dollars for the clinic where the embryos are frozen (70).

In Europe, a donor egg process can cost between 7,000 and 8,000 Euros, and a frozen embryo transfer between 1,200 and 3,000 Euros (71), (72), (73); maintenance of cryopreserved embryos is around 200 Euros annually (73).

EMBRYO ADOPTION AGENCIES

The use of agencies for frozen embryo adoption is rare in Europe, but common in the United States (66).

One of the services provided by these agencies is to help the couple donating the embryos to find the ideal family for their embryos, taking care of the legal requirements



and above all respecting the privacy of the information provided (66). Some agencies are only concerned with providing information to their clients so that they can make the best choice, while others actively participate in the selection process.

Another service offered by the agencies is to help resolve any conflicts that may arise, either because the donor couple have different criteria for donation, or because of differences between the adoptive couple. They also advise the adoptive parents, if they wish, about the best procedure to guarantee the efficiency of the technique in their specific case (74).

There are many websites that provide comprehensive information on all matters related with adoption, especially in the United States (74), (75), (76), (77), and also others that provide information on Institutions that offer frozen embryo adoption, always with a positive spirit, and with the ultimate aim of encouraging potential adoptive parents to adopt (78).

CONCLUSION

There is a great number of frozen human embryos currently, a situation that is not compatible with their dignity. Therefore, we must find a solution to this unfair situation.

The ultimate solution is to not produce more embryos than are to be implanted, because then there would be no surplus of embryos to freeze. If this is not achieved, and the number of frozen embryos continues to increase, four solutions can be taken to solve this problem: a) using them for biomedical experiments; b) having them adopted by their biological parents; c) having them adopted by other couples to build a family d) keeping them frozen indefinitely. Undoubtedly, solution a) is the most ethical, but it is not always possible, so adoption by a couple, different from the biological parents, is a possible real solution.

BIBLIOGRAPHY

1. Gianaroli L, Geraedts J, Veiga A, et al. The “Father of IVF” and a founding father of ESHRE. *Human Reproduction*. 2010; 25(12): 2933-2935.
2. ESHRE. The world’s number of IVI and ICSI babies has now reached a calculated total of 5 millions. [Online].; 2012 [cited 2015 February. Available from: <http://www.eshre.eu/Press-Room/Press-releases/Press-releases-ESHRE-2012/5-million-babies.aspx>.



3. de Mouzon J, Goossens V, Bhattacharya S, et al. Assisted reproductive technology in Europe, 2006: results generated from European registers by ESHRE. *Human Reproduction*. 2010; 25(8): 1851-1862.
4. de Mouzon J, Goossens V, Bhattacharya S, Castilla JA, Ferraretti AP, Korsak V, et al. Assisted reproductive technology in Europe, 2007: results generated from European registers by ESHRE. *Human Reproduction*. 2012; 27: 954-966.
5. Ferraretti AP, Goossens V, de Mouzon J, Bhattacharya S, Castilla JA, Korsak V, et al. Assisted reproductive technology in Europe, 2008: results generated from European registers by ESHRE. *Human Reproduction*. 2012; 27: 2571-2584.
6. Ferraretti AP, Goossens V, Kupka M, Bhattacharya S, de Mouzon J, Castilla JA, et al. Assisted reproductive technology in Europe, 2009: results generated from European registers by ESHRE. *Human Reproduction*. 2013; 28: 2318-2331.
7. Kupka MS, Ferraretti AP, de Mouzon J, Erb K, D'Hooghe T, Castilla JA, et al. Assisted reproductive technology in Europe, 2010: results generated from European registers by ESRHE. *Human Reproduction*. 2014; 29: 2099-2113.
8. Hoffman D, Zellman G, Fair C, et al. Cryopreserved embryos in the United States and their availability for research. *Fertility and Sterility*. 2003; 79: 1063-1069.
9. Casey SB. The frozen waiting to be chosen: Human embryo adoption in America. *The Christian Lawyer*. 2007; 3(2): 12-15.
10. Dayal MB. Indications for egg and embryo donation. In *Principles of Oocyte and Embryo Donation*. New York: Springer-Verlag; 1998. 19-22.
11. Marquez W. El limbo de los embriones congelados. *BBC Mundo*. 2011 November 19.
12. HFEA. [Online].; 2013 [cited 2013 February 7. Available from: www.hfea.gov.uk.
13. Boscia FM. L'adozione per la nascita degli embrioni non più impiantabili. *Newsletter di Scienza & Vita*. 2012; 58: 17-18.
14. Nadal Pedreña J, Franquets del Castillo. Número de embriones congelados en España hasta finales del 2010. In Nadal Pedreña J. *Donación de embriones*. Salerno (Italia): Momento Médico SRL; 2013. 319-324.
15. Riggs R, Mayer J, Dowling-Lacey D, et al. Does storage time influence postthaw survival and pregnancy outcome? An analysis of 11,768 cryopreserved human embryos. *Fertility and Sterility*. 2010; 93: 109-115.
16. Revel A, Safran A, Laufer N, et al. Twin delivery following 12 years of human embryo cryopreservation: Case report. *Human Reproduction*. 2004; 19: 328-329.
17. López Teijón M, Serra O, Olivares R, et al. Delivery of a healthy baby following the transfer of embryos cryopreserved for 13 years. *Reproductive Biomedicine Online*. 2006; 13: 821-822.



18. Reed ML, Hamic A, Caperton CL, Thompson DJ. Live birth after anonymous donation of twice-cryopreserved embryos that had been stored in liquid nitrogen for a cumulative storage time of approximately 13.5 years. *Fertility and Sterility*. 2010; 94: 2771.e1-3.
19. Riggs R, Mayer J, Dowling-Lacey D, Chi TF, Jones E, Oehninger S. Does storage time influence postthaw survival and pregnancy outcome? An analysis of 11,768 cryopreserved human embryos. *Fertility and Sterility*. 2010; 93: 109-115.
20. Sutcliffe AG. *Follow-up of children conceived from cryopreserved embryos*. *Molecular and Cellular Endocrinology*. 2000; 169: 91-3.
21. Wennerholm UB, Söderström-Anttila V, Bergh C, Aittomäki K, Hazekamp J, Nygren KG, et al. Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. *Human Reproduction*. 2009; 24: 2158-2172.
22. Wennerholm UB, Söderström-Anttila V, Bergh C, Aittomäki K, Hazekamp J, Nygren KG, et al. Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. *Human Reproduction*. 2009; 24: 2158-2172.
23. Cohen IG, Adashi EY. Made-to-order embryos for sale. A brave new world? *The New England Journal of Medicine*. 2013; 368: 2517-2519.
24. Zarembo A. An ethics debate over embryos on the cheap. *Los Angeles Times*. 2012 November 19.
25. Armora E. La crisis lanza la adopción de embriones. *ABC*. 2011 Sept 11.
26. Murphy TF. Dignity, marriage and embryo adoption: a look at Dignitas Personae. *Reproductive Biomedicine Online*. 2011; 23: 860-868.
27. American Society for Reproductive Medicine. Disposition of abandoned embryos: a committee opinion. *Fertility and Sterility*. 2013; 99: 1848-1849.
28. Asch R. High pregnancy rates after oocyte and embryo donation. *Human Reproduction*. 1992; 7: 734.
29. Keenan, Fingeer R, Check J, et al. Favorable pregnancy, delivery and implantation rates experienced in embryo donation programs in the United States. *Fertility and Sterility*. 2008; 90: 1077-1080.
30. Center for Disease Control and Prevention. Assisted reproductive technology (ART) report. National summary report. [Online].; 2010 [cited 2012 June 20. Available from: <http://apps.nccd.cdc.gov/art/Apps/NationalSummaryReport.aspx>.
31. Roque M, Lattes S, García de Jesús S, et al. Fresh embryo transfer versus frozen-thawed embryo transfer in assisted reproduction in techniques cycles: a systematic review and meta-analysis. European Society of Human Reproduction and Embryology (ESHRE) Congress. 2012.



32. Wang YA, Sullivan ED, Black D, et al. Pre-term birth and low birth weight after assisted reproductive technology-related pregnancy in Australia between 1996 and 2000. *Fertility and Sterility*. 2005; 83: 1650-1658.
33. Belva F, Henriët S, van den Abbeel E, et al. Neonatal outcome of 937 children born after transfer of cryopreserved embryos obtained by ICSI and IVF and comparison with outcome data of fresh ICSI and IVF cycles. *Human Reproduction*. 2008; 10: 2227-2238.
34. Zhu D, Zhang J, Cao S, et al. Vitri-fied -warmed blastocyst transfer cycles yield higher pregnancy and implantational rates compared with fresh blastocyst transfer-time for new embryo transfer strategy? *Fertility and Sterility*. 2011; 95: 1691-1695.
35. Wikland M, Hardarson T, Hillensjo , et al. Obstetric outcomes after transfer of vitri-fied blastocysts. *Human Reproduction*. 2010; 25: 1699-1707.
36. Aflatoonian A, Moghaddam FM, Mashayekhy M, Mohamadian F. Comparison of early pregnancy and neonatal outcomes after frozen and fresh embryo transfer in ART cycles. *Journal of Assisted Reproduction and Genetics*. 2010; 27: 695-700.
37. Maheshwari A, Pandey S, Shetty A, et al. Obstetric and Perinatal outcomes in singleton pregnancies resulting from the transfer of frozen thawed versus fresh embryos generated through in-vitro fertilisation treatment. A systematic review and meta-analysis. *Fertility and Sterility*. 2012; 98: 368-377.
38. Tesarik J, M JA, Hazout A, Aubriot FX, Nathan C, Cohen-Barcricie P, et al. Embryos with high implantation potential after intracytoplasmatic sperm injection can be recognized by a simple, non-invasive examination of pronuclear morphology. *Human Reproduction*. 2000; 15: 1396-9.
39. Van Royen E, Mangelshtots K, De Neubourg D, Laurelys I, Ryckaert G, Gerris J. Calculating the implantation potential of day 3 embryos in women younger than 38 years of age: a new model. *Human Reproduction*. 2001; 16: 326-32.
40. Racowsky C, Ohno-Machado L, Kim J, Biggers JD. Is there an advantage to scoring embryos on more than 1 day? *Human Reproduction*. 2009; 24: 2104-13.
41. Cummings J, Breen T, Harrison K, Shaw JM, Wilson LM, Hennessey JF. A formula for scoring human embryo growth rates in in vitro fertilization: its value in predicting pregnancy in comparison with visual estimates of embryo quality. *Journal of In Vitro Fertilization and Embryo Transfer*. 1986; 3: 284-95.
42. Ceyhan ST, Jackson KV, Racowsky C. Selecting the most competent embryo. In Carrell DT, Racowsky C, Schegel PN, Van Coorhis BJ, editors. *Biennial review of infertility*, vol 1. New York: Humana Press; 2009. 143-69.
43. Stokes PJ, Hawkhead JA, Fawthrop RK, Picton HM, Sharma V, Leese HJ, et al. Metabolism of human embryos following cryopreservation: Implications for the



- safety and selection of embryos for transfer in clinical IVF. *Human Reproduction*. 2007; 22: 829-835.
44. Edgar D, Archer J, McBain J, Bourne H. Embryonic factors affecting outcome from single cryopreserved embryo transfer. *Reproductive Biomedicine Online*. 2007; 14: 718-723.
 45. LEY 14/2006. LEY 14/2006, de 26 de mayo, about Técnicas de Reproducción Humana Asistida. BOE. 2006 May 27; nº 126.
 46. Embryo donation and abortion. What's the Difference Between the Terms Donation and Adoption? Embryo Adoption Awareness Center. [Online].; 2014 [cited 2015 February. Available from: <http://www.embryo adoption.org/donors/terminology-defined.cfm>.2014.
 47. López Teijón M. Donación y adopción de embriones. In Nadal Pedreña J. *Donación de embriones*. Salerno (Italia): Momento Médico SRL; 2013. 189-193.
 48. Burke D. Embryo Adoption Act. Model legislation & policy guide for the 2011 legislative year. Americans United for Life. 2010;; 1-10.
 49. Ethics and Law Advisory Committee paper. Donation review - conditional donation. [Online].; 2011 [cited 2014 February 5. Available from: http://www.hfea.gov.uk/docs/2011-06-08_ELAC_paper_-_conditional_donation.pdf.
 50. American Society for Reproductive Medicine. The Ethics Committee of the American Society for Reproductive Medicine. American Society for Reproductive Medicine: defining embryo donation. *Fertility and Sterility*. 2009; 92: 1818-1819.
 51. Trounson A, Freeman L. El uso de la criopreservación de embriones en el programa FIV. *Clinical Obstetrics and Gynecology*. 1985; 12: 825-833.
 52. Lutien P, Trounson A, Lenton J, et al. The establishment and embryo donation in a patient with primary ovarian failure. *Nature*. 1984; 307: 174-5.
 53. Bustillo M, Buster J, Cohen S, et al. Non-surgical ovum transfer as a treatment in infertile women. *The Journal of the American Medical Association*. 1984; 251: 1171-1173.
 54. Blakeslee S. Infertile woman has baby through embryo transfer. *The New York Times*. 1984 February 4.
 55. Collard C, Kashmeri S. “De embriones congelados a siempre familias”: Ética del parentesco y ética de la vida en la circulación de embriones entre las parejas donantes y las adoptantes en el programa Snowflakes. *Revista de Antropología Social*. 2009; 18: 43-65.
 56. IVF Australia. Embryo donation. ; 2013.
 57. Goedeke S, Payne D. Embryo donation in New Zealand: a pilot study. *Human Reproduction*. 2009; 24: 1939-1945.



58. López Teijón M, Serra O, Olivares R, et al. Delivery of a healthy baby following the transfer of embryos cryopreserved for 13 years. *Reprod Biomed Online*. 2006; 13: 821-822.
59. Monía N. Ya son diez los bebés nacidos mediante el programa de Adopción de Embriones. [Online].; 2006 [cited 2015 February. Available from: www.institutomarques.com/www.cimaclinic.com/mayo 2006.
60. Martín Mora P. La “adopción” de embriones. Escritura pública. En sociedad. Adopción de embriones. [Online].; 2007 [cited 2015 February. Available from: <http://www.notariado.org/publicaciones/escritura/numeros45/21.htm>.2007.
61. Alvarez-Diaz JA. Embryo donation in developing countries. *Gaceta Médica de México*. 2010; 146: 228-241.
62. Monía N. Nace un niño de un embrión congelado hace 13 años. [Online].; 2006 [cited 2006 May 31. Available from: www.institutomarques.com/www.cimaclinic.com/.
63. Embryo Adoption Awareness Center. Embryo Quality: Chosen Life Embryo Adoption. Awareness Center (A). [Online].; 2013 [cited 2015 February. Available from: <http://www.embryo-adoption.org/adopters/videos.cfm>.2013.
64. Nightlight Christian Adoptions. Nightlight Christian Adoptions. Snowflakes embryo adoption program. Frequently asked questions by adopting families. [Online].; 2014 [cited 2015 February. Available from: <http://www.nightlight.org/faqs/#b6>.
65. Snowflakes embryo adoption and donation. Snowflakes Embryo Adoption “Nightlight Christian Adoptions”. [Online].; 2013 [cited 2015 February. Available from: <http://www.nightlight.org/snowflakes-embryo-adoption/2013>.
66. Embryo Adoption Agencies. For Adoption Agencies. Embryo Adoption. Awareness Center. [Online].; 2014 [cited 2015 February. Available from: <http://www.embryo-adoption.org/adoption-agencies/index.cfm>.2014.
67. Coroleu B, Luna M, Rodríguez-Purata J, et al. Preparación endometrial: ciclo natural o ciclo con preparados hormonales en la donación de embriones. In Nadal Pedreña J. *Donación de embriones*. Salerno (Italia): Momento Médico SRL; 2013. 175-182.
68. Monía N. Datos comunicados al Dr Reginald Furger en comunicación particular. [Online].; 2010 [cited 2010 September 2. Available from: www.institutomarques.com.
69. Iriberry A. Adoptar un embrión para ser madre. *elmundo.es*. 2013 March 5.
70. Cost of embryo adoption. Cost of Embryo Adoption. Embryo Adoption Awareness Center. [Online].; 2014 [cited 2015 February. Available from: http://www.embryo-adoption.org/donors/cost_of_embryo.adoption.cfm.2014.
71. Sahuquillo MR. Padres pero no genéticos. *El País*. 2013 August 16.



72. Tapia C. Madre de 600 criaturas. *Diario de León.es*. 2013 July 22.
73. Pessina A. Personal communication. 2011 September.
74. Webinar Archives. Awareness Center Webinars: Registration is requested for each attendee. Embryo Adoption. Awareness Center. [Online].; 2014 [cited 2015 February]. Available from: <http://www.embryooption.org/education/webinar-registration.cfm>.
75. Adopter FAQs. Adopter FAQ. Embryo Adoption. Awareness Center. [Online].; 2014 [cited 2015]. Available from: http://www.embryooption.org/adopters/adopting_parent_fac.cfm.2014.
76. Donors. Donor FAQs. Embryo Adoption Awareness Center. [Online].; 2014 [cited 2015 February]. Available from: <http://www.embryooption.org/donors/faqs.cfm>.2014.
77. Adopters. The process for Adopting Embryos. Embryo Adoption Awareness Center. [Online].; 2014 [cited 2015 February]. Available from: <http://www.embryooption.org/adopters/index.cfm>.2014.
78. Personal Stories. Personal Stories. Embryo Adoption Awareness Center. [Online].; 2014 [cited 2015 February]. Available from: http://www.embryooption.org/donors/personal_stories.cfm.2014.

