Ethical aspects of AGE banking

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Chapter 13: Ethical aspects of AGE banking

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Abstract Despite the original opposition against oocyte banking for healthy women, AGE banking has found its way to the clinic rather fast. This does however not mean that the ethical debate regarding the desirability of AGE banking is settled. In this chapter, the arguments that have been used on both sides of the debate are critically assessed. While it is difficult to build a consistent argument against allowing AGE banking in the given context in which infertility treatment and oocyte banking for cancer patients are widely supported, concerns regarding proper introduction into the clinic cannot be dismissed as easily.

1. Introduction

Although the first healthy live birth from a frozen human egg cell dates back to 1986, egg freezing has long been so inefficient that it was hardly considered a valid treatment option (Gook, 2011). However, with improvements in both the slow freezing technique and ultra-rapid cooling by vitrification, oocyte cryopreservation (OC) has become an efficient procedure with high survival rates after thawing (Cobo et al, 2008; Noyes et al, 2009; Noyes et al, 2010; Almodin et al., 2010; Grifo and Noyes, 2010; Rienzi et al., 2010; Trokoudes et al., 2011).

The primary application of this new technology was to bank eggs for women who are at risk of losing their fertility due to cancer, cancer treatment or other grave illnesses. However, not only cancer patients are at risk of losing their fertility, but all women in their late thirties are. Therefore, also for this group, OC could be beneficial. However, the expansion of the option of OC for 'medical reasons' to OC

for ‘non-medical reasons’, ‘social reasons’ or ‘anticipated gamete exhaustion’ (AGE-banking) (Stoop et al, 2014) was not met with the same enthusiasm. In 2007, the American Society for Reproductive Medicine (ASRM) stated that “Oocyte cryopreservation is an experimental procedure that should not be offered or marketed as a means to defer reproductive aging, primarily because data relating to clinical outcomes are limited. […] However, unlike healthy women, [women with cancer or other illnesses requiring immediate treatments that seriously threaten their future fertility] may have no viable options and therefore may be appropriate candidates for such treatment despite its experimental status” (ASRM 2007). The European Society for Human Reproduction and Embryology (ESHRE) took a similar stand: “In view of the lack of success and clinical applications in the case of ovarian tissue, this application should not be offered to women as a means to preserve their fertility potential when there is no immediate threat to their fertility. According to similar reasoning, oocyte freezing for fertility preservation without a medical indication should not be encouraged.” (ESHRE, Shenfield et al. 2004). Given the explosion of new research data in the years that followed, several authors have called directly upon ASRM and ESHRE for a less restrictive attitude (Homburg, van der Veen et al. 2009; Rybak and Lieman 2009). This resulted in a revision of the ESHRE-guidelines in 2012, now stating that “[i]n the light of new scientific developments, and after considering relevant ethical arguments […] oocyte cryopreservation to improve prospects of future child bearing should also be available for non-medical reasons” (ESHRE, 2012). The ASRM, however, despite lifting the ‘experimental’ label from OC for medical purposes in 2012, maintained its stance that OC should not be offered for non-medical reasons due to a lack of data for this specific indication and due to the fact that “[m]arketing this technology for the purpose of deferring childbearing may give women false hope and encourage women to delay childbearing” (ASRM, 2012).

In this chapter, the different arguments pro and con OC to counter age-related fertility decline will be presented and critically assessed. This overview will show that although there are no strong arguments against the principle of AGE-banking, the ethical concerns that are voiced in regard to the technology do point at legitimate concerns about the way it is / should be offered to patients. As a

preliminary remark, please note that although safety is obviously an important ethical concern for all new medical technology, it will not be discussed in this chapter.

2. Fundamental objections against AGE banking

2.1. The argument from nature

A first set of fundamental objections against AGE-banking relate to the idea that this technology pushes the boundaries of nature. The age at which the average woman becomes infertile is then not merely labelled as a biological fact, as the age at which women *can* no longer have children, but rather as the age at which women *should* no longer have children. In ethical theory, this phenomenon is known as the is-ought fallacy. Unless if one starts from the religious belief that everything was created for a clear purpose and that we live in the best of all possible worlds, the (average) natural state of things does not teach us anything about how things ought to be. This also implies that there is no obvious reason why medical interventions should be limited to preserving or restoring the natural state of things – as is done in 'medical' egg freezing – and should not be used to counter natural phenomena that have a negative impact on our wellbeing. It should be remarked that many illnesses are age-related, just as the decline in female fertility, and that many medical interventions are performed to solve inconveniences that may be considered 'normal' if they occur at a certain age. In fact, not much of modern day medicine would remain, if we were to cancel all interventions for age-related health problems. Yet, nobody seems to be opposed to the treatment of Alzheimer's disease or osteoporosis. The distinction between medical and non-medical egg freezing based on the idea that aging is not a medical problem is therefore problematic. If we have good reasons to counteract infertility for women with a desire for parenthood, then it matters little what the cause of the pending infertility is.

Also, besides the fact that the distinction between medical and non-medical OC is irrelevant, it is also a false distinction in the sense that there is a grey area in between these two applications (Stoop et al, 2014). For instance, should women who request OC due to a prognosis of unexplained premature ovarian insufficiency be regarded as freezing for medical or non-medical reasons? Even for cancer patients, certain regimens of radiation or chemotherapy will lead to immediate sterility in

(reproductively speaking) older women, but not in younger women. The reasons for the former to store oocytes are therefore both disease-related and age-related. In this chapter, I will maintain the term 'AGE banking', which allows for a wide interpretation, although many of the objections discussed will be aimed primarily at egg freezing for healthy women.

2.2. Medicalization

A related objection against AGE-banking is that it provides a medical solution for a problem that in essence is not a medical problem, but a societal one, namely the steady rise in women's age at first childbirth (now on average between 25 and 35 years old). This can then be attributed either to the woman herself or to the way the labour market is structured.

If women are held accountable for 'delaying' childbearing due to 'lifestyle choices', the non-medical alternative to OC is obvious and simple: women should reproduce earlier. This is however easier said than done. The most important reason for banking eggs in healthy women is the lack of a partner (Nekkebroeck et al, 2010; Baldwin et al, 2015; Hodes-Wertz et al., 2013). Should we thus encourage women to become single mothers? Should we advise them not to wait for Mr. Right, but go for Mr. Good Enough? Besides the most important factor of finding a suitable partner to share parenthood with, several studies have found that women also find it increasingly important to first complete their education, have financial security and good housing before taking on the responsibility of parenthood (Lampic et al., 2006; Maheshwari et al., 2008). These are not trivial desires, but relevant for the wellbeing of themselves and their future children. Bonneux et al. (2008) have therefore argued that the rise in the age at first childbirth is a trend that increases overall wellbeing and that should not be regretted in itself, even if it is regrettable that the peak of natural female fertility does not coincide with the moment at which women would preferably have their children.

Alternatively, rather than holding women accountable for the rising age at first childbirth, society might be blamed, in the sense that many women experience difficulties in starting a parental project during their reproductive lifespan due to professional obligations. While fertility preservation can offer a solution to this problem once it presents itself, it does not tackle the root cause. As mentioned

by Goold and Savulescu (2009), "one might ask whether we actually help women […] by taking for granted their bad employment situation and offering them egg freezing to deal with it". Fertility preservation for social reasons is then a type of unnecessary medicalization of society that can be avoided by creating a better social climate for working mothers. However, societal change takes time. While we might attempt to tackle the (hypothetical) root cause of delayed childbearing by making it easier for young parents (both women *and* men) to combine personal and professional responsibilities, this is unfortunately not a solution for women who are in their late thirties and involuntarily childless today. Therefore, long term solutions to the benefit of future generations should not prevent us from offering practical solutions to the present generation (Dondorp & de Wert, 2009; Mertes, 2013). Moreover, keeping in mind that lack of a partner is the primary reason to request AGE banking, we should be sceptical that reforms in the labour market will reduce the demand for AGE banking. At the same time, we should remain vigilant that the option of AGE banking is not invoked as an excuse to invest less in reforms in the labour marked that enable a better combination of professional and parental obligations.

2.3. A negative impact on society

Related to the argument that women's employment situation does not allow them to reproduce at a young age, there is a concern that the offer of AGE banking will increase the pressure on women to invest in their careers while they are young at the expense of pursuing parenthood. This concern became especially convincing when Facebook and Apple announced that they would start offering OC to their female employees. As argued elsewhere, even if AGE banking in itself may not be ethically problematic, the offer by employers is (Mertes, 2015). For such a policy to be implemented with respect for women's reproductive autonomy, a substantial number of conditions need to be fulfilled, which can be reduced to three categories: (1) women should understand the benefits, risks and limitations, (2) women should feel no pressure to take up the offer; (3) the offer should have no negative effect on other family-friendly policies and should in fact be accompanied by such policies. Fulfilling these conditions may turn out to be impossible. Thus, regardless of companies' possible good intentions, women's reproductive autonomy is not well served by offering them company-sponsored AGE banking.

Another concern is that the offer of AGE-banking may cause an increase in the average age at which women become mothers. Although this effect is possible, there are various reasons why it is unlikely that this effect would be significant. First, the number of women opting to bank oocytes is likely to remain a small fraction of all women desiring to become mothers, as the procedure requires a substantial physical and financial effort. Second, it is wrong to assume that these women make a choice between reproducing 'now' or reproducing a couple of years later. For many of the women opting for AGE banking, reproducing at the moment of freezing is not an option (due to lack of a partner, as mentioned). The more likely alternatives are thus either not reproducing at all, or reproducing via donor oocytes. Third, women who bank oocytes on average do so in their late thirties and on average consider the maximum age to use the oocytes below 44 years (Stoop et al, 2015). This means that even for the small fraction of women who would consider a pregnancy at the time of freezing if AGE banking were not available, motherhood is only 'deferred' for about 5 years. In conclusion, the most likely effect of offering fertility preservation to healthy women is not a decline in the number of young mothers but a small incline in the number of older mothers. Whether an increase in the age of mothers is problematic in itself, is discussed in chapter 12.

3. Fundamental arguments for AGE banking

3.1. Gender equality

An argument in favour of AGE banking is that this intervention is emancipatory in nature as it can fix the factual discrimination between men and women in regard to their reproductive lifespan: if men are able to conceive children at an advanced age, then women should have the same liberty. This is again an example of the is-ought-fallacy. The mere biological fact that a 70-year old man is capable of conceiving children, says nothing about the moral reasons for (not) doing so. However, as reproductive freedom is highly valued in our society, we do not impose forced sterilization on men above a certain age. Reproduction at an advanced age is thus a liberty right, but that does not mean that it is also a claim right. That means that if an infertile senior citizen (male or female) applies for IVF treatment, it may not be granted based on considerations regarding the welfare of the future child. Given the fact that

pregnancy complications are an additional concern in the case of women, a lower cut-off age in ART for women than for men may be justified.

3.2. Reproductive autonomy

The main argument for AGE banking is that it increases reproductive autonomy. Due to this new technology, women are theoretically able to extend their reproductive lifespan and are thus less dependent on donor oocytes if they wish to reproduce at an age at which their ovarian reserves are depleted (see below). As mentioned above, the age at which women desire to have children rises and not all women succeed in finding a partner with whom to share parenthood before the decline of their fertility. When single, childless women reach their late thirties and still want to become mothers, they – unlike men – are under pressure to find a partner fast and embark on parenthood with that new partner fast, or resort to single parenthood. AGE banking can relieve women of this pressure by offering them a couple more years to find a suitable partner, thus allowing for more autonomous choices. Caveats are that only a limited number of oocytes can be banked, so that a pregnancy – let alone a live birth – can certainly not be guaranteed and that women still face legal restrictions on the age until which they can use their banked oocytes to (try to) establish a pregnancy.

An absolute prerequisite for AGE banking to positively influence reproductive autonomy is that women receive correct information about the possibilities and limitations. The overly optimistic portrayal of AGE banking as 'insurance against infertility' or as a means to defer childbearing while retaining fertility misguides women about the limitations. If a woman with a very strong desire for parenthood would defer childbearing relying on banked oocytes and subsequently fails to achieve a pregnancy with those banked oocytes, her reproductive autonomy was very ill-served by AGE banking.

3.3. Psychological benefit

Linked to reproductive autonomy and the pressure on finding a suitable partner when a woman approaches the end of her reproductive lifespan is the observation that women may not only derive a clinical benefit (the chance of conceiving a child), but also a psychological benefit from knowing that there is still 'a chance' for her to have children, regardless of whether she ever actually uses her stored

eggs. Research by Stoop et al (2015) shows that even women who have banked oocytes but have never used them or no longer envisage using them do not regret their decision to bank and would do so again in similar circumstances. Also, some women decide a couple of years after banking that they will embark on single parenthood although their preferential life plan involved building a family with a partner. Banking then allowed them some extra time to consider the option of single parenthood without Damocles' sword hanging above their heads.

3.4. Self-donation

A strong argument for allowing AGE banking is that it is in fact a form of oocyte donation which does not involve a third party (Knopman et al., 2010; Rybak and Lieman, 2009). If a woman is currently unable to conceive due to a depletion of her ovarian reserve, she can establish a pregnancy with donor oocytes, but there are some drawbacks to this option. First, the resulting child will not have a genetic connection with the mother. Although this is not necessarily problematic, it is a suboptimal option for many people, either because they identify parenthood with genetic parenthood (or at least presuppose that one is 'more' of a parent when there is a genetic connection) or because they fear a disruption of their family unit if the donor would claim a role or if the child would regard the donor as the 'real' mother (Wyverkens et al, 2015). Second, oocyte donation requires that a healthy woman is subjected to ovarian stimulation and oocyte retrieval. These are unpleasant and time-consuming procedures with (limited) risks involved, which hold no benefit for the woman who is subjected to these risks. Both donor anonymity and open identity donation are potentially problematic for the donor, in the former case because she might want to know the person resulting from her donation, in the latter case because she might *not* want to be contacted by that person. As we currently allow donor conception despite these drawbacks, it would be inconsistent not to allow a woman to donate oocytes to her future self. In this case the genetic link is maintained and the person subjected to the risks of ovarian stimulation is the same person as the one who reaps the benefit of (potential) parenthood. The only dissimilarity that might be invoked to justify a different approach is that in the case of 'regular' oocyte donation, the need for a donor oocyte is present, whereas when a woman decides to bank oocytes for future use, she can never be certain that there will ever be an actual need. Therefore, the effort might be in vain.

4. Concerns about improper introduction into the clinic

4.1. Utility

The major problem for AGE banking is that in many cases, it will be a medical intervention without clinical benefit. Few women will mimic the best case scenario – which is the one that commercial companies offering AGE banking are most likely to highlight – in which women between 30 and 35 realise that they will not be in ideal circumstances to reproduce in the coming years, store their oocytes, then meet Mr. Right, build up a stable relationship and come back to the clinic to use their oocytes around age 40 (when their ovarian reserve is depleted), establish a pregnancy and become mothers. If women bank their oocytes at a younger age, the quality of these oocytes – and therefore the chance to achieve a healthy live birth – is better, but then there is a large chance that they will never return to use them, as there is still a big chance that they will be able to reproduce naturally during their reproductive lifespan. If women bank their oocytes at an older age, there is a larger chance that they might need them (in the sense that their window of opportunity for natural reproduction is about to close), but the odds of each oocyte to lead to a live birth is a lot smaller as the quality will be a lot poorer (Mertes and Pennings, 2011). In practice, it turns out that most 'AGE bankers' correspond more to the latter category. Women do not proactively freeze eggs during their twenties or early thirties in a well thought-out plan of achieving their career goals first and focussing on parenthood later. Instead, women turn to AGE banking as a last resort. This also means that many women present themselves at the clinic at a moment when the intervention can bring little benefit for them because ovarian stimulation may only yield a couple of bad quality oocytes which are unlikely to lead to a viable pregnancy.

Although it is too early to draw any definitive conclusions, preliminary studies indicate that the eventual utility of the procedure may indeed be low. For example, Garcia-Velasco et al. (2013) report that from 560 non-oncological patients banking oocytes between 2007 and 2012, only 30 had returned for treatment in 2013 and of those 30 there were 5 live births and 8 on-going pregnancies at the time of publication. In a study by Stoop et al. (2015) only half the women who banked oocytes anticipates using them in the future. However, this study also confirms that besides the clinical utility of achieving a live

birth, there is also a psychological benefit to consider, as the great majority of women was still positive about the decision to store oocytes, also if they anticipate not using them. In any case, counselling for women who inquire about the possibility of oocyte banking should include information about the possibly low utility of the procedure and thus of their investment.

4.2. Information

Not only information about utility needs to be provided to potential oocyte bankers, but also, as previously argued, information about the success rates, stratified by age (Mertes & Pennings, 2011). Ideally, not the chance of a live birth per oocyte should be given, but the cumulative live birth rate with the number of oocytes that are expected to be banked. This information is however not always available. Cil et al. (2013) have constructed a model for the age specific probability of live-birth for different numbers of thawed oocytes (based on a meta-analysis) and report a probability of live-birth for a 38-year old woman (at the time of freezing) of 15% for 6 thawed oocytes (after vitrification). 37-38 has been reported as the average age of women opting for AGE-banking (Gold et al., 2006; Klein et al., 2006; Sage et al., 2008; Nekkebroeck et al., 2010; Vallejo et al, 2013; Baldwin et al, 2015). It is clear that for this group, metaphors such as 'putting fertility on ice', 'stopping the reproductive clock', 'fertility insurance' or 'fertility preservation' are misleading, as the chance that they will not be able to conceive with their banked oocytes appears to be larger than the chance that they will succeed.

Also for younger women, the danger of misinformation is lurking. Although there are currently few reports of young women storing oocytes with the explicit aim of postponing motherhood, some commercial companies are definitely aiming at young women invested in their careers to 'sell' their intervention to, targeting them through events such as egg freezing parties. In this situation, the danger is that women do not realise that postponing parenthood always results in a decline in the chance of establishing a pregnancy, even when eggs are banked, as these banked eggs are always limited in number. A woman may thus enter into AGE banking believing that her desire for children is 'safe',

while it is not. According to the model by Cil et al, a 28 year old women would have a 27% live birth rate for 6 thawed oocytes (after vitrification).

4.3. Misleading and coercive offers

Concerns regarding the clinical utility and the provision of information are both linked to the commercialisation of autologous oocyte banking. When financial profit becomes a factor that influences the offer of oocyte banking or even becomes the goal, the probability that women's attention will be drawn to the drawbacks or that they will be encouraged to reconsider their plans of banking is low. Reference is easily made to reproductive autonomy in this context: if women want to bank their oocytes – even despite the low utility – they should have the liberty to do so and therefore commercial companies should be free to offer it to them. However, respecting an autonomous choice requires that the choice is truly autonomous, that is, that it is based on all the relevant information and free from outside pressure. This is more easily achieved in a non-commercial context.

Besides the fear for misleading offers by commercial egg banking companies, fears exist regarding coercive offers by employers. As discussed above (see 2.3), even if the rationale behind including egg banking in a benefit package would be to increase reproductive autonomy, the chance that the opposite – a decrease in reproductive autonomy – would result is very large.

4.4. Access

If employers cannot include egg banking in their healthcare benefit package, then how should egg banking be financed? If the banking woman pays, there are concerns about distributive justice in the sense that this technology will only be available to the segment of society that can afford it. However, allocating public healthcare funds to AGE banking is not straightforward either, given the fact that healthcare funding is limited and should thus be allocated to the most urgent healthcare needs. Also, the limited utility is an argument against incorporating AGE banking in publicly funded healthcare. Cost-efficiency is also a relevant factor to be considered here. However, as argued elsewhere (Mertes and Pennings, 2012), in a system where IVF is reimbursed, it would be inconsistent to cover IVF treatment with donor oocytes for women who are infertile due to aging, but not with their own previously banked

oocytes. Thus, in such a context, at least the second part of the procedure, that is thawing, fertilising and transferring any resulting embryos, should be reimbursed. This does not necessarily imply that the first step of the procedure, namely the costs related to ovarian stimulation, oocyte retrieval, oocyte freezing and storage need to be covered, although there are good reasons to argue for full coverage, a cash back-system or more free transfer cycles (Mertes and Pennings, 2012).

5. Conclusion

Despite the original opposition against AGE banking for healthy women, AGE banking has found its way to the clinic rather fast. One reason for this evolution may be that a number of the initial ethical objections to oocyte freezing for so-called 'social' or 'non-medical' reasons were not very convincing, especially given the contrast with the warm welcome oocyte banking received in the field of oncofertility. The arguments that we should not try to circumvent natural boundaries, solve societal problems with medical solutions or that AGE banking will have a negative impact on society are either flawed or only partially convincing. On the other side of the debate, the argument that we should allow AGE banking to combat gender inequality in terms of the maximal age at childbirth was dismissed, but the argument that women's reproductive autonomy should be respected, that this technology may not only clinically, but also psychologically benefit patients and that it is inconsistent to support egg donation by others, but not autologous egg donation appear to carry some weight.

However, even if there are good arguments to bring AGE banking to the clinic, a cautious approach is warranted. First of all, the utility of the procedure may be low and women may be overly optimistic about their chances of conceiving after AGE banking. They should therefore be properly counselled and sufficiently informed about their personal chances of success. Misleading information by commercial companies and coercive offers from companies to their female employees are to be avoided and finally, reflection is needed on access to the technology and on the extent in which reimbursement by public healthcare is desirable.

Key message

1. The distinction between oocyte cryopreservation for medical reasons or non-medical/social reasons is ill-founded.

2. In principle, oocyte cryopreservation for healthy women could increase reproductive autonomy and benefit women both clinically and psychologically.

3. The biggest ethical concerns are linked to the implementation in the clinical context.

4. Proper counselling aimed at insuring realistic expectations towards the success rate of the procedure and countering misleading information is a necessary condition that should be guaranteed at all times.

5. Reflection is need on access to the technology.

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