Oocyte or embryo donation to women of advanced reproductive age: an Ethics Committee opinion

Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

Advanced reproductive age (ARA) is a risk factor for female infertility, pregnancy loss, fetal anomalies, stillbirth, and obstetric complications. Oocyte donation reverses the age-related decline in implantation and birth rates of women in their 40s and 50s and restores pregnancy potential beyond menopause. However, obstetrical complications in older patients remain high, particularly related to operative delivery and hypertensive and cardiovascular risks. Physicians should perform a thorough medical evaluation designed to assess the physical fitness of a patient for pregnancy before deciding to attempt transfer of embryos to any woman of advanced reproductive age (>45 years). Embryo transfer should be strongly discouraged or denied to women of ARA with underlying conditions that increase or exacerbate obstetrical risks. Because of concerns related to the high-risk nature of pregnancy, as well as longevity, treatment of women over the age of 55 should generally be discouraged. This statement replaces the earlier ASRM Ethics Committee document of the same name, last published in 2013 (Fertil Steril 2013;100:337–40). (Fertil Steril® 2016;106:e3–7. ©2016 by American Society for Reproductive Medicine.)

Key Words: Ethics, third-party reproduction, complications, pregnancy, parenting

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KEY POINTS

- Oocyte and embryo donation is an established standard of practice for the treatment of age-related infertility and is associated with high rates of pregnancy success.
- Adverse obstetrical events and outcomes are associated with advanced reproductive age (ARA), particularly related to operative delivery, hypertensive disorders, gestational diabetes, and perinatal mortality.
- Women of ARA considering oocyte or embryo donation should undergo comprehensive medical testing focused on ascertaining cardiovascular and metabolic fitness, as well as a psychosocial evaluation to determine if adequate supports are in place to raise a child to adulthood.
- Prospective ARA patients should be counseled about the increased medical risks related to pregnancy, and that many of these risks are poorly characterized due to lack of data. The counseling process should involve the participation of a physician familiar with managing high-risk pregnancy.
- Oocyte and embryo donation should be strongly discouraged if underlying medical conditions that could further increase the obstetrical and neonatal risks are present, particularly hypertension or diabetes.
- In view of the limited data regarding maternal and fetal safety, as well as concerns related to longevity and the need for adequate psychosocial supports for raising a child to adulthood, providing donor oocytes or embryos to women over 55 years of age, even when they have no underlying medical problems, should be discouraged.
- Multiple pregnancy significantly increases the risks associated with pregnancy and delivery; therefore, elective single embryo transfer (eSET) is the preferred method of treatment in ARA women.
- Prospective older parents should be counseled regarding short- and long-term parenting and child-rearing issues specific to their age. The age and health of the partner, if present, should also be considered in this discussion.
- It is ethically permissible for programs to decline to provide treatment to women of ARA based on concerns over the health and well-being of the patient and offspring.

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Reprint requests: Ethics Committee, American Society for Reproductive Medicine, 1209 Montgomery Hwy, Birmingham, Alabama 35216 (E-mail: ASRM@asrm.org).

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The reported success of oocyte donation to women in their 50s (1, 2) and early 60s (3, 4) suggests that pregnancy may be possible in virtually any woman with a normal

uterus, regardless of age and even in the absence of ovaries and ovarian function. A woman's reproductive lifespan, once a dictate of nature, now can be artificially extended using hormone therapy and oocyte or embryo donation, or in other cases using autologous cryopreserved eggs or embryos procured from earlier treatment cycles. In the United States nearly 20,000 embryo transfers using either fresh or frozen donated eggs or embryos occur annually, and often to women of ARA.

Oocyte donation to younger women with primary ovarian insufficiency, gonadal dysgenesis, poor oocyte quality, or diminished ovarian reserve falls into the conventional realm of medical treatment addressing the needs of individuals suffering from pathological conditions. However, the practice of oocyte and embryo donation is more ethically challenged when it is used as treatment for women who have experienced natural menopause. The average age of spontaneous menopause in the United States is about 52 years, an age at which most women neither desire nor expect to have children. Nonetheless, circumstances may lead some women beyond the natural age of menopause to request oocyte or embryo donation. For example, women with no children may find life partners in their 50s and desire to start a family, or older couples in second marriages may wish to have children together. In other cases, the loss of a child may motivate couples to seek fertility care. Women may wish to transfer cryopreserved embryos from a prior in vitro fertilization (IVF) cycle performed years before menopause occurred. Is the use of a technology that extends women's reproductive life beyond the age of natural menopause so unreasonable as to be denied, and, if not, should a recommended standard of practice for its application be defined?

ARGUMENTS IN FAVOR OF OOCYTE AND EMBRYO DONATION TO WOMEN OF ADVANCED REPRODUCTIVE AGE

Arguments in favor of oocyte and embryo donation to ARA women are based on medical efficacy and safety, societal practices, gender equality, and reproductive freedom. Live-birth rates per embryo transfer in women undergoing egg and embryo donation are generally above 50% (5). Practices throughout the United States offering assisted reproduction typically provide donor oocytes and embryos, making services readily accessible. In our society, it is not unusual for children to be raised by grandparents who take on most of the parenting role and often bring economic stability, parental responsibility, and maturity to the family unit. There is, therefore, no reason to assume that society will be harmed by allowing ARA individuals to procreate, or that older women and their partners lack the physical and psychological stamina for raising children. Also, older men may naturally father children and are not restricted from assisted reproductive care when seeking fertility services. Therefore denying ARA women a successful alternative for reproduction at ages equivalent to men appears prejudicial. Finally, our society respects the rights of individuals to make reproductive choices regardless of age or life expectancy. For example, individuals with life-limiting illnesses are not prohibited from reproduction because of their shortened life expectancy. Given the possibility that postmenopausal reproduction may satisfy the strong desire of a couple or individual for offspring, it would be wrong to deny women the use of donated oocytes or embryos solely because of their age.

ARGUMENTS AGAINST OOCYTE AND EMBRYO DONATION TO WOMEN OF ADVANCED REPRODUCTIVE AGE

Arguments against oocyte and embryo donation to ARA women are based on ideas about natural limits to reproduction, concerns about childrearing, longevity, and medical risks. Biologic naturalism contends that oocyte and embryo donation to older women breaches the "natural" limit to reproductive capacity in humans and that limited reproductive abilities defined by aging is intrinsic to being human. Thus, to transcend this limit is "unnatural." According to this view, the fact that some grandparents successfully raise children would not necessarily be sufficient to justify using assisted reproductive technologies to establish pregnancies after menopause.

Another concern relates to the belief that ARA women and their partners may be unable to meet the emotional, financial, and physical demands of raising a child and maintaining a long-term parental relationship. In addition, there is a greater likelihood with older parents that the children will suffer the loss of one or both parents before reaching adulthood (6). Data on obstetrical and neonatal outcomes associated with pregnancy after age 50 remain preliminary and concerns have been raised that the risks to mother and child are too great to justify the provision of oocytes or embryos to ARA women. Opponents to providing oocytes or embryos to women in their 50s and older argue that pregnancy at this age serves neither the interests of older women, nor the interests of the children they bear.

MEDICAL AND OBSTETRICAL ISSUES

The medical and obstetrical risks associated with oocyte or embryo donation to women following natural menopause are still largely preliminary because of the limited amount of published data. It is well established that medical and obstetrical complications are significantly increased in pregnant women over the age of 45 years, especially regarding adverse events occurring as a result of hypertensive disorders and diabetes (7, 8). One report on the US experience with donor oocyte cycles from 1996–98 included 440 cycles with recipients aged 50–54 (9) but did not assess maternal complications of pregnancy. High rates of pregnancy-induced hypertension, gestational diabetes, and cesarean sections in recipients over 50 years old have also been noted (2, 10–13). In one series of 45 live births delivered by healthy women aged 50–63 who established pregnancy with donated oocytes, 35% experienced pregnancy-induced hypertension, 20% developed gestational diabetes, and 78% underwent a cesarean section (11). The risks were even higher in women more than 55 years old, compared with those 50–54 years old. For example, the risk of pregnancy-induced

hypertension was 26% in the 50–54 age group, but increased to 60% in patients over 55 years of age. Only case reports describe the outcome of pregnancies in women over age 60 years (3). Multiple gestations increase obstetrical and neonatal risk at all ages, and it is particularly important to avoid in ARA women. In a report of obstetrical outcomes in recipients 45 years and older, it was suggested that the high rate of multiple pregnancies (39.2%) was a large contributing factor to the high rate of antenatal complications (14). Accordingly, increased use of multifetal pregnancy reduction procedures has occurred in women over age 45 (15).

The effect on the offspring of ARA mothers conceiving through oocyte and embryo donation is even less clear and under-reported. Some studies suggest a higher risk of low birth weight and fetal mortality in women over 50 years old (16) while others show risks to be similar to those of younger women undergoing oocyte donation (17, 18).

In general, the incidence of genetic abnormalities in the offspring of women undergoing oocyte and embryo donation relates to the age of the oocyte donor and not to that of the gestating mother. However, concerns have been raised that children conceived in this manner may face uncertain genetic risks when the male partner is older in age. Defining advanced paternal age is complicated and no clear agreement exists as to an age threshold for suggesting a higher risk to offspring (19). However, although relatively rare events, advanced paternal age has been associated with disabilities and disorders resulting from single-gene mutations and chromosomal abnormalities (20, 21), new dominant mutations resulting in congenital anomalies (22), and an increased risk of autism (23) and schizophrenia (24) in offspring. Clinical data have been difficult to evaluate because maternal age often increases along with that of the male partner. When oocytes from a young woman are donated, the impact of paternal age on abnormalities in the offspring can be inferred. Two small studies suggest that fertilization, pregnancy, and live-birth rates, and the risks of abnormalities of the offspring when the male partner is over age 50, are identical to those with younger male partners when donor oocytes are provided (25, 26).

Potential medical consequences may be minimized by treating only healthy ARA women and following the standard of practice of using eSET in order to eliminate multiple-birth gestations. It is recognized that focusing on women over the age of natural menopause is rather arbitrary, but age-related medical complications of pregnancy likely follow a continuum of increasing risk. As for other assisted reproductive technology (ART) candidates for whom pregnancy poses particular and elevated risks to health, providers are obligated to thoroughly and systematically evaluate the magnitude of risks to the patient in pregnancy and beyond and to counsel patients about these concerns. Inclusion of a physician experienced in the care of high-risk obstetrical patients in the processes of preconception evaluation and counseling is the best means to assure that these objectives are met. It is ethically permissible for physicians to decline to provide treatment to ARA women who have underlying medical or psychosocial conditions that may likely increase obstetrical, neonatal, and child-rearing risks.

PARENTING ISSUES

Any serious discussion of the ethics of pregnancy at ARA must focus on considerations of parenting and child support, especially in couples where there is only one parent or when both partners are older. Concerns include the possibility that one or both parents could die before the child reaches adulthood, the stresses of parenting as an older parent, and the difficulties of meeting the emotional and physical demands of parenting.

Parental loss is one of the most stressful life events for children or adolescents to endure (27). Although a 50-year-old Caucasian woman in the United States has a life expectancy of over 80 years, on average, it is more likely that a woman who conceives at 50 rather than at 30 will die before her child reaches adulthood. The age and health of the partner and his or her life expectancy should therefore be discussed when considering oocyte and embryo donation procedures. Under these circumstances, many of the children born from oocyte and embryo donation may not have siblings or extended family to support them after losing their parents and may feel both physically and emotionally abandoned.

Very few studies have been published about parenting in women who conceived and delivered after natural menopause. The limited data, however, do not support concerns that older parents have reduced parenting capacity. Indeed, the greater financial and emotional stability older parents often offer (28) may be an advantage to children. Mental and physical functioning scores, as well as parenting stress in women over age 50 receiving donated eggs, were the same as in younger women undergoing the same treatment (29). Certainly, further studies are needed on the subject of parenting in the sixth decade of life and beyond before the psychological and social impact on children can be fully assessed.

Gestational carrier arrangements have been proposed as a means to bypass the obstetrical and neonatal risks associated with pregnancy in ARA patients. These proposals should also be evaluated carefully. If ARA women have underlying medical disorders that render gestating a pregnancy too risky, then they also are more likely to have significant physical impairments or die before their children reach adulthood.

ADDITIONAL CONSIDERATIONS AND SUMMATION

A central ethical issue is whether the interests of women and children are well served by the use of ART technology in this manner. These interests may be realized when the desire for a child and the ultimate bearing and rearing of a child contribute to mutual well-being. The Committee believes that many ARA women, particularly in the age range of 45–54, are healthy and well prepared for parenting, and therefore are reasonable candidates to receive donated oocytes and embryos.

Infertility is an expected characteristic of menopause. The Committee believes that achieving a pregnancy through oocyte and embryo donation after the occurrence of natural menopause is not such a significant departure from other currently accepted fertility treatments as to be considered

ethically inappropriate. However, physicians may not agree with extending fertility care to ARA women due to the high-risk nature of pregnancy and uncertainties of childrearing, and the Committee respects the right of practices not to offer care and to refer such requests elsewhere.

The medical risks to the mother and child are of paramount concern, but it will be many years before adequate data are available to objectively evaluate these issues fully. Although the data on pregnancy outcome in older mothers and couples remain scant, the risks of gestational diabetes and pregnancy-induced hypertension in otherwise healthy women are significantly higher as the age of mothers increases and are particularly high after age 55. In most cases, however, these pregnancy-related complications are not severe enough to compromise the long-term health of women and their ability to care for children. A careful medical evaluation and age-appropriate health screenings should be performed before proceeding to treatment. Oocyte and embryo donation should be strongly discouraged if ARA patients have underlying medical problems that will further increase their obstetrical or neonatal risks. Prospective parents should be counseled to expect greater risks for obstetrical complications. Substantial caution should be exercised when considering these procedures, even in healthy older women, since many of these medical problems are uniquely gestational. Because obstetrical and neonatal risks may be directly related to or increased by the occurrence of multiple gestations, eSET is recommended in all ARA patients.

Finally, psychosocial counseling of ARA couples considering oocyte and embryo donation should include discussions of short- and long-term parenting and childrearing. The health and age of the partner, if present, should be considered in these discussions. It is also ethically permissible for programs to decline to provide treatment to ARA women based on these concerns (30).

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Judith Daar, J.D.; Jean Benward, M.S.W.; Lee Collins, J.D.; Joseph Davis, D.O.; Leslie Francis, Ph.D., J.D.; Elena Gates, M.D.; Elizabeth Ginsburg, M.D.; Sigal Klipstein, M.D.; Barbara Koenig, Ph.D.; Andrew La Barbera, Ph.D., H.C.L.D.; Laurence McCullough, Ph.D.; Richard Reindollar, M.D.; Mark Sauer, M.D.; Rebecca Sokol, M.D., M.P.H.; Sean Tipton, M.A.; Lynn Westphal, M.D.

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