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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 St

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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 highrisk 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 childrearing 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 wellbeing of the patient and offspring.

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

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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. Livebirth 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 pregnancyinduced 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

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