

SUCCESSFUL DELIVERY AFTER AGE 50: A REPORT OF TWO CASES AS A RESULT OF OOCYTE DONATION

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Background: Because of donor oocyte programs, women who previously were considered too old to successfully achieve conception and delivery can now bear children. To our knowledge, there have been no previous reports of pregnancy outcome in women over age 50 who conceived using donor oocytes. This study presents the pregnancy and delivery data on two women who delivered at age 52.

Cases: Case 1 was a 51-year-old woman, gravida 3, para 3, whose three children had been conceived with her first husband more than 20 years previously. She had remarried 18 years before presentation and had been actively trying to conceive for the last 7 years. She was diagnosed as being in menopause based on elevated gonadotropins, amenorrhea, and failure to have progesterone-withdrawal menses. She conceived on her first embryo transfer cycle with embryos derived from donor oocytes and fertilized by her husband's sperm (oocytes were donated by a woman who was undergoing retrieval for in vitro fertilization). During pregnancy she remained healthy, but had uterine prolapse at 20 weeks. She delivered a normal healthy male at 40.5 weeks; cesarean was performed because of a presumptive diagnosis of fetal distress after 3 hours of labor, when monitoring revealed fetal heart decelerations. Case 2 was also a 51-year-old woman, gravida 6, para 4, who wished to conceive with her second husband's sperm through the donor oocyte program. She had amenorrhea of 2 years' duration and elevated gonadotropins. Conception occurred after fertilization of a donor oocyte by her husband's sperm. She had an uneventful pregnancy, but labor was induced at 38 weeks' gestation given the supposed high-risk status of this age group. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively.

Conclusion: Theoretically, the risks of pregnancy complications in older patients are magnified given the aging maternal cardiovascular system, which may predispose these women to placental insufficiency. These first two cases of donor oocyte pregnancies in women over age 50 found no maternal or fetal age-related complications. We hope these reports will encourage all researchers to share their findings so that prospective patients can make better, more informed decisions as to whether they want to participate in donor oocyte programs. (*Obstet Gynecol* 1993;81:835-6)

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The advent of donor oocyte programs has allowed functionally agonadal women the opportunity to become pregnant and deliver.¹⁻⁵ We recently reported a high success rate in establishing pregnancies in women over age 40 using donor oocytes.⁶ This led to speculation that women of more advanced age might also conceive and give birth.⁷ However, few data exist on the maternal or fetal risks associated with a maternal age over 50 years.

We report the establishment of pregnancy in two women, both 51 years of age, at different institutions using similar methodology. To our knowledge, their deliveries are unique in representing the oldest patients in this country to deliver after oocyte donation. However, we believe that others even older will inevitably follow.

Case Reports

Case 1

A 51-year-old woman, gravida 3, para 3-0-0-3, requested pregnancy through oocyte donation at the University of Medicine and Dentistry of New Jersey. Her previous three children had been conceived with her first husband. She had remarried 18 years before presentation and had been trying unsuccessfully to conceive for the past 7 years. She had experienced menopause approximately 1 year before, with documented elevated serum gonadotropins and amenorrhea. The patient was in good health; the only abnormality was a uterine prolapse with descensus of the cervix to within 1 cm of the introitus on Valsalva maneuver.

We initiated hormone replacement using a sequential regimen of oral micronized estradiol and intramuscular progesterone as previously described.⁶ Timed endometrial biopsy was performed while the woman was taking replacement hormones. Semen analysis and culture of the husband was within normal limits.

Oocytes were obtained from a woman undergoing standard in vitro fertilization who chose to donate her supernumerary eggs. The patient was synchronized to the cycle of the woman undergoing ovarian hyperstimulation, as previously described.⁸ Oocytes were retrieved by transvaginal aspiration. Twelve oocytes were donated and eight fertilized. Five pre-embryos (2PN, 3, 4, 2, 4 cells) were transcervically transferred, and pregnancy was confirmed 11 days later.

The patient was maintained on hormone replacement for 102 days into the pregnancy. During gestation she gained 27 lb, but experienced no complications such as diabetes, hypertension, or proteinuria. Uterine prolapse requiring intermittent bed rest occurred at 20 weeks' gestation. Ultrasound at 6 and 10 weeks showed normal growth. Amniocentesis revealed a 46,XY fetal karyotype. At 36 weeks, she was treated with bed rest for return of the prolapse. Nonstress test was reactive.

At 40.5 weeks' gestation, she spontaneously went into labor with contractions documented to occur every 5 minutes. At 4 cm of cervical dilation and after 3 hours of labor,

pronounced fetal decelerations were noted with slight meconium-stained amniotic fluid. A presumptive diagnosis of fetal distress prompted an emergency cesarean, which was performed under regional anesthesia. The male infant weighed 3545 g and had Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. Neonatal examination was entirely normal. Both mother and infant were discharged on postpartum day 5.

Case 2

The woman, gravida 6, para 4-0-2-4, presented at age 51 requesting oocyte donation at the University of Southern California. Her previous four children had been conceived with her first husband. She had remarried 15 years before presentation and had been trying to conceive for approximately 5 years. Amenorrhea and hot flashes had occurred 2 years before, and she was prescribed hormone replacement therapy. Medical health studies were within normal limits.

Oocytes were obtained from a 27-year-old donor who underwent a standard regimen of ovarian hyperstimulation followed by transvaginal aspiration.⁸ Seventeen oocytes were aspirated, ten were fertilized, and five four-cell pre-embryos were transcervically transferred. Pregnancy was confirmed 9 days after embryo transfer. The woman was kept on hormone replacement consisting of oral micronized estradiol 2 mg/day and intramuscular progesterone 100 mg/day for the first 14 weeks' gestation.

Over the course of the pregnancy, the woman gained a total of 60 lb, 35 lb gained by 14 weeks' gestation. Serial ultrasound examinations demonstrated appropriate fetal growth. A glucose tolerance test performed at 20 weeks was normal. The woman continued to be active throughout her pregnancy and remained normotensive with no signs or symptoms of hypertensive disease. At 38 weeks' gestation, examination revealed an inducible cervix with a Bishop score of 7. Given the presumed high-risk status of women in this age group, we began oxytocin induction with the placement of an epidural anesthetic. Labor progressed well, with delivery of a vigorous 3000-g male infant 5.5 hours after the initiation of oxytocin. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively, and the neonatal examination was entirely normal. The placenta weighed 770 g and demonstrated no abnormality on review. Postpartum, both mother and infant did well and were discharged on the second day.

Discussion

To our knowledge, these cases represent the oldest women in the United States to deliver as a result of oocyte donation. Although the feasibility of establishing pregnancy in women of this advanced reproductive age has been confirmed, the wisdom of doing so will undoubtedly be challenged. Both women were in excellent health and were evaluated thoroughly before embryo transfer for medical problems known to complicate pregnancy. Both were apprised of the unknown risks associated with pregnancy at this age and accepted the potential complications. Our decision to proceed

with both couples was dependent not only on their good physical and psychological health, but also on the demonstrable stability of their marriages and incomes.

The risk of complications of pregnancy in an older woman are at least theoretically magnified given the aging maternal cardiovascular system, which may predispose these women to placental insufficiency. Though using oocytes from younger women relieves the anxiety of the increased risk of chromosomal abnormalities, eg, trisomies, only careful evaluation and reporting of clinical outcomes will allow us to better determine the true risks in these older patients. As more data accrue, 50+-year-old patients will be able to make more informed decisions about whether to consider oocyte donation. As new cases are reported, some age limit may be found above which there is a significantly increased risk to mother and/or fetus.

References

1. Sauer MV, Paulson RJ. Human oocyte and preembryo donation: An evolving method for the treatment of infertility. *Am J Obstet Gynecol* 1990;163:1421-4.
2. Formigli S, Roccio C, Belotti G, Stangalini A, Coglitore MT, Formigli G. Oocyte donation by gamete intra-fallopian transfer to amenorrhoeic and cycling patients given replacement steroids. *Hum Reprod* 1989;4:772-6.
3. Cha KY, Koo JJ, Ko JJ, Choi DH, Han SY, Yoon TK. Pregnancy after in vitro fertilization of human follicular oocytes collected from nonstimulated cycles, their culture in vitro and their transfer in a donor oocyte program. *Fertil Steril* 1991;55:109-13.
4. Asch RH, Balmaceda JP, Ord T, Borrero C, Rodriguez Rigau LJ, Rojas FJ. Gamete intra fallopian transfer (GIFT) and oocyte donation—a novel treatment for infertility in premature ovarian failure. *Gynecol Endocrinol* 1987;1:105-11.
5. Sauer MV, Paulson RJ, Lobo RA. Simultaneous establishment of pregnancies in two ovarian failure patients using one oocyte donor. *Fertil Steril* 1989;52:1072-3.
6. Sauer MV, Paulson RJ, Lobo RA. A preliminary report on oocyte donation extending reproductive potential to women over 40. *N Engl J Med* 1990;323:1157-60.
7. Angell M. New ways to get pregnant. *N Engl J Med* 1990;323:1200-2.
8. Meldrum DR, Wisot A, Hamilton F, Gutlay AL, Kempton W, Huynh D. Routine pituitary suppression with leuprolide before ovarian stimulation for oocyte retrieval. *Fertil Steril* 1989;51:455-9.

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