Pregnancy following Oocyte Donation and in vitro Fertilization after Failed Attempts at Donor Uterine Lavage

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Key Words
In vitro fertilization
Donor ovum transfer
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Abstract
Pregnancy was successfully established in an agonadal woman using donated oocytes and in vitro fertilization. The oocyte donor had previously failed to provide an in vivo fertilized pre-embryo to the infertile couple despite several attempts at uterine lavage.

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Introduction
Successful impregnations of functionally agonadal women have been reported using donated ova obtained through in vitro fertilization, gamete intrafallopian transfer, and uterine lavage [1–3]. Although preliminary, methods permitting ovarian hyperstimulation of donors may increase the probability of conception in the female recipient [2], since the likelihood of transferring a fertilized ovum is enhanced [4].

Herein we report the establishment of pregnancy in a castrate patient despite prior failed attempts at donor ovum transfer via uterine lavage. Oocytes were obtained by transvaginal ultrasound-directed aspiration of a self-selected donor. The ova donor previously underwent 3 cycles of uterine lavage and elected to attempt in vitro fertilization after endometritis developed following a uterine flushing.

Case Report
The patient, now pregnant, is a 31 year-old woman, gravida 0, who 7 years previously had been rendered castrate following bilateral oophorectomies for a ruptured appendix. After physical and psychological screening, she was placed on ovarian steroid replacement of 17ß-estradiol (Estrace, Mead Johnson and Co, Evansville, Ind., USA) and progesterone (Eli Lilly, Indianapolis, Ind., USA), as previously described [3]. Following documentation of a normal, in-phase, late secretory endometrium (day 26), she was synchronized with the menstrual cycle of a 32-year-old gravida 2, para 1, abortion 1 ovum donor chosen by the recipient couple. The donor underwent uterine lavage following insemination with washed semen on 3 separate occasions over 4 months, as previously reported [4]. A total of 9 lavage procedures were performed during the clinical trial. A morula was recovered 96 h after ovulation in the first attempt at uterine flushing, but all subsequent lavage attempts failed to retrieve any ova. The transferred morula did not result in pregnancy. During
the third series of uterine flushing, a thick, mucopurulent discharge was noted. An endometrial biopsy was performed, demonstrating acute endometritis. The patient was placed on antibiotics and remained asymptomatic. Because of this infection, the donor was not considered a candidate for further uterine lavages. She elected a trial of in vitro fertilization. Synchronization was established by the recipient beginning Estrace 3 days prior to the donor’s ovarian stimulation with human menopausal gonadotropin (hMG; Pergonal, Serono Laboratories, Randolf, Mass., USA), with stepwise increases in the dose of Estrace until the day of human chorionic gonadotropin injection (table 1). To prevent the occurrence of a premature luteinizing hormone (LH) surge leuprolide (Lupron, TAP Pharmaceutical, North Chicago, Ill., USA) was administered to the donor prior to and concomitantly with hMG. Four oocytes were recovered by transvaginal ultrasound-guided needle aspiration without anesthesia using parenteral analgesia consisting of meperidine hydro-chloride (Demerol; Winthrop Laboratories, New York, N.Y., USA) and midazolam hydrochloride (Versed; Roche Laboratories, Nutley, N.J., USA). The procedure was well tolerated, lasting 15 min. Four oocytes fertilized and three cleaved. Forty-eight hours after aspiration, three 4-cell ova were transferred. Serum β-human chorionic gonadotropin (β-hCG) level 14 days after transfer was 315 mlU/ml, using the First International Reference Preparation standard. Two weeks later, with a β-hCG of 14,400 mlU/ml, two gestational sacs were visualized. Despite this, only one embryo developed. Estrace and progesterone support was discontinued 100 days after transfer when estradiol and progesterone levels were noted to be increasing independent of the administered dose of medication.

Discussion
We previously reported pregnancies occurring after nonsurgical transfer of a fertilized ovum from the uterus of a donor to the uterus of an infertile patient [3, 4]. This method has been successful in infertility patients with and without gonadal function. Although the lavage procedure efficiently retrieves ova, complications include retained pregnancies and endometritis in the donor (3%). Furthermore, in vivo blastocyst production and ovum yield among fertile donors is highly variable, making the likelihood of retrieving a transferable fertilized ovum at best approximately 33% [5].

Reports of pregnancies in agonadal women following ovarian hyperstimulation of oocyte donors implies an enhanced pregnancy rate (20–75%) over that obtained using spontaneously ovulating donors [2, 6]. With the advent of transvaginal aspiration techniques, a nonsurgical approach to in vitro fertilization is now possible, making it a reasonable option for donors willing to undergo ovarian hyperstimulation. Furthermore, the probability of obtaining ova from

Table 1. Synchronizing oocyte donor to recipient with ovarian failure

<table>
<thead>
<tr>
<th>Donor</th>
<th>Recipient</th>
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<tr>
<td>hMG 3 ampules daily beginning on day 2 of menstrual cycle</td>
<td>Estrace 3 days prior to hMG given to donor: days 1–5, 0.5 mg twice daily; days 6–9, 1 mg twice daily; days 10–13, 2 mg three times daily; days 14–100, 1 mg twice daily</td>
</tr>
<tr>
<td>micromized estradiol begun 3 days before hMG given to donor</td>
<td>hCG 10,00 IU/ml when follicles measure 16–18 mm in diameter</td>
</tr>
<tr>
<td>progesterone 50 mg i.m. given the day after hCG administered to donor, then twice a day for 100 days</td>
<td>progesterone 50 mg i.m. given the day after hCG administered to donor, then twice a day for 100 days</td>
</tr>
</tbody>
</table>

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a single aspiration is high, limiting donor involvement as well as reducing risks from repetitive
procedures. Although uterine lavage is performed without anesthesia or analgesia, we have found
transvaginal aspiration to be very well tolerated by donors.
In conclusion, ovarian hyperstimulation and transvaginal ultrasound-directed oocyte aspiration of
oocyte donors offers an attractive alternative to women willing to participate in an ovum
donation program. As illustrated by this case, a single procedure commonly results in the
obtainment of ova for transfer, limiting donor involvement and reducing risks.

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