

# Defective oocytes are not a common cause of unexplained infertility as determined by evaluation of sharing oocytes between infertile donors and recipients

**B. Katsoff<sup>1</sup>, J.H. Check<sup>2</sup>, J. Mitchell-Williams<sup>2</sup>**

<sup>1</sup>Temple University School of Medicine, Department of Medicine, Philadelphia, PA

<sup>2</sup>Cooper Medical School of Rowan University, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ (USA)

## Summary

**Purpose:** To determine if defective oocytes or sperm may be a common etiologic factor in unexplained infertility. **Materials and Methods:** A retrospective comparison of fertilization rates and pregnancy rates from infertile donors with unexplained infertility trying to conceive with in vitro fertilization-embryo transfer (IVF-ET) and their respective recipients, who shared the other half of the oocytes with the recipient's male partner for financial compensation was performed. Pregnancy rates from donors and recipients were also compared to other donor recipient pairs sharing oocytes from infertile donors with tubal or male factor or financially-compensated donors providing oocytes to two recipients. **Results:** Pregnancy rates from infertile donors with unexplained infertility were comparable not only to their respective recipients but to other donor/recipient pairs that received oocytes from donors with tubal or male factor or financially-compensated donors. Fertilization rates were somewhat reduced in the infertile donors. **Conclusions:** Abnormal embryos resulting from an oocyte or sperm defect do not appear to be a common cause of unexplained infertility. The possibility does exist that sperm may be an etiologic factor in reduced fertilization potential, which not only could be obviated by conventional oocyte insemination, but could be further improved by intracytoplasmic sperm injection (ICSI).

**Key words:** Oocyte sharing; Infertile donors; Oocyte recipients; Fertilization rates; Pregnancy rates.

## Introduction

Sometimes a definitive cause for infertility is not identified or an infertility factor seems to be corrected but a successful pregnancy does not ensue. This group is considered to have unexplained or cryptic infertility [1]. Theoretically the problem could be defective oocytes despite the appearance of achieving follicular maturation and oocyte release, defective sperm despite normal semen parameters, defective tubal function despite the appearance of normal fallopian tubes, or some endometrial factor inhibiting implantation.

Defective oocytes or sperm may manifest in a few ways: either failing to fertilize the oocyte, or fertilizing the oocyte but failure to develop into an embryo or failure for a normal-appearing embryo to implant. Theoretically in vitro fertilization-embryo transfer (IVF-ET) by either exposing the oocyte to many more sperm or performing intracytoplasmic sperm injection (ICSI) may overcome the problem of defective fertilization of sperm or oocyte in some circumstances. However, it would not be expected to overcome problems of the creation of an abnormal embryo if there was a defective oocyte or sperm causing that problem.

Of course IVF-ET would be expected to be successful in cases where defective tubal function is the cause of the problems. IVF-ET may not be successful for cases of endometrial factor.

IVF-ET has been successful in cases of unexplained infertility. Nevertheless, a priori, based on the theoretical circumstances of defective oocytes or sperm leading to embryos of low implantation potential and the possibility of an endometrial factor, IVF-ET would not seem to be as likely to produce a live baby in cases of unexplained infertility, as compared to tubal or male factor problems unless the infertility factors requiring the need for more sperm and oocyte contact or the need to circumvent the fallopian tubes are the main factors involved in unexplained infertility.

It has been demonstrated that when infertile donors are used to provide oocytes for recipients requesting donor oocytes, these oocytes are equally as effective in establishing normal pregnancies as oocytes from financially-compensated donors [2]. However, many couples are reluctant to choose infertile oocyte donors with unexplained infertility for fear of poor quality oocytes preferring donors whose infertility was related to tubal or male factor problems.

There were two objectives of this retrospective comparison of pregnancy rates in women who are infertile vs their respective recipients: 1) Determine how likely are defective oocytes or defective sperm in creating embryos that do not implant as etiologic factors in unexplained infertility? 2) How effective are oocytes from infertile donors in establishing pregnancies in recipients when originating from donors with unexplained infertility vs oocytes from infertile donors with tubal disease or male factor vs financially-compensated donors?

Revised manuscript accepted for publication June 18, 2012

Table 1. — *Pregnancy rates of oocyte donors based on their infertility types in shared IVF cycles.*

Donor Infertility Type Type of Insemination	Unexplained			Male factor			Tubal		
	Total	ICSI	Conventional	Total	ICSI	Conventional	Total	ICSI	Conventional
No. retrievals	21	5	16	96	86	10	212	77	135
No. transfers	10	2	8	61	56	5	138	53	85
No. with 0% fertilization	2	0	2	4	3	1	1	0	1
No. with 1% but < 50% fertilization	5	0	5	10	10	0	37	9	28
% with low fertilization	33.3	0.0	43.8	14.6	15.1	10.0	17.9	11.7	21.5
No. clinical pregnancies	6	2	4	32	28	4	67	24	43
% clinical pregnancies	60.0	100.0	50.0	52.5	50.0	80.0	48.6	45.3	50.6
No. viable (12 weeks)	6	2	4	29	25	4	62	22	40
% viable transfers	60.0	100.0	50.0	47.5	44.6	80.0	44.9	41.5	47.1
No. spontaneous abortion (SAB)	0	0	0	4	4	0	8	3	5
% SAB / clinical pregnancies	0.0	0.0	0.0	12.5	14.3	0.0	11.9	12.5	11.6
No. deliveries	6	2	4	28	24	4	59	21	38
% delivered	60.0	100.0	50.0	45.9	42.9	80.0	42.8	39.6	44.7
No. embryos transferred	24	7	17	165	152	13	377	142	235
Avg. no. embryos transferred	2.4	3.5	2.1	2.7	2.7	2.6	2.7	2.7	2.8
No. sacs implanted	10	4	6	50	44	6	105	36	69
Implantation rate	41.7	57.1	35.3	30.3	28.9	46.2	27.9	25.4	29.4

## Materials and Methods

A retrospective review of all donor oocyte cycles over a 12-year time period was made where oocytes were shared between two partners. The infertile donor shared oocytes in exchange for sharing financial obligations. There were two types of oocyte donors: ones that were infertile sharing half the oocytes with a recipient and using the other half to perform IVF-ET themselves and financially-compensated recipients providing oocytes for two recipients.

The infertile donors were divided into three groups according to the infertility etiology: unexplained infertility, male factor, and tubal factor. Clinical (ultrasound evidence of pregnancy at eight weeks), live-delivered pregnancy rates, and implantation rates were compared according to etiology of infertility in the infertile donor vs their respective donor oocyte recipients. Clinical and live-delivered pregnancy rates and implantation rates were also compared amongst infertile donors according to their type of infertility.

Comparisons of pregnancy and implantation rates were also made between the various recipients according to the etiology of the infertility in the infertile donors or whether they used a financially-compensated donor. The data was also stratified according to whether ICSI was performed or not.

## Results

The pregnancy and implantation rates in infertile oocyte donors according to the etiology of their infertility are seen in Table 1.

The pregnancy and implantation rates in recipients according to the etiology of infertility in the infertile donors or if the source of oocytes was from financially-compensated donors are seen in Table 2.

The fact that the live-delivered pregnancy rates for infertile donors with unexplained infertility was 60.0% vs 53.3% for recipients receiving oocytes from infertile donors with unexplained infertility suggests that subtle oocyte or sperm defects leading to normal-appearing embryos that do not implant is not a common etiologic factor for unexplained infertility (Tables 1 and 2).

The rarity of defective oocytes or sperm despite normal appearance in unexplained infertility is further substantiated by not finding lower pregnancy rates in the infertile donor with unexplained infertility compared to donors with male factor or tubal factor Table 1.

The live-delivered pregnancy rate of 43.7% (113/236) for recipients using oocytes from infertile donors was not significantly different from the 47.9% (356/743) found from those using financially-compensated donors confirming previous smaller studies [2].

These data found that two of 16 (12.5%) of the infertile donors with unexplained infertility had failed fertilization compared to only one of 85 (1.2%) with tubal factor ( $p = 0.06$ , Fisher's exact test). None of the 12 recipients receiving oocytes from infertile donors failed to fertilize any oocytes ( $p = 0.52$ , Fisher's exact test).

The group with the largest percentage of low fertilization rates with conventional insemination amongst infertile donors was the group with unexplained infertility (43.8%), compared to 10.0% for male factor, and 21.5% for tubal factor (Table 1). However, amongst recipients, there were similar rates of low percentage fertilization ranging from 17.6% to 22.2% in recipients according to type of infertility of infertile donors and recipients receiving oocytes from financially-compensated donors.

## Discussion

These data clearly show that defective oocytes or defective sperm leading to the formation of normal-appearing embryos that do not implant is not a very common cause of unexplained infertility based on the comparable pregnancy rates in donors and recipients receiving oocytes from infertile donors with unexplained infertility. This conclusion is supported by the fact that oocytes from infertile donors with unexplained infertility led to comparable pregnancy rates in both donors and recipients compared to other infertility etiologies in the other infertile donors and even compared to financially-compensated donors.

Table 2. — Pregnancy rates of oocyte recipients based on their infertility types of the oocyte donors in shared IVF cycles or whether they were financially compensated.

Donor Infertility Type Type of Insemination	Unexplained			Male Factor only			Tubal			Paid egg donor		
	Total	ICSI	Conv. Insem.	Total	ICSI	Conv. Insem.	Total	ICSI	Conv. Insem.	Total	ICSI	Conv. Insem.
No. retrievals	21	12	9	96	54	42	212	105	107	945	553	392
No. transfers	15	8	7	78	46	32	143	71	72	743	427	316
No. with 0% fertilization	0	0	0	1	0	1	5	2	3	13	6	7
No. with 1% but < 50% fertilization	2	0	2	13	6	7	37	17	20	103	41	62
% with low fertilization	9.5	0.0	22.2	14.6	11.1	19.0	19.8	18.1	21.5	12.3	8.5	17.6
No. clinical pregnancies	9	3	6	40	24	16	86	39	47	416	238	178
% clinical pregnancies	60.0	37.5	85.7	51.3	52.2	50.0	60.1	54.9	65.3	56.0	55.7	56.3
No. viable (12 weeks)	8	3	5	31	18	13	79	36	43	377	211	166
% viable transfers	53.3	37.5	71.4	39.7	39.1	40.6	55.2	50.7	59.7	50.7	49.4	52.5
No. spontaneous abortion (SAB)	1	0	1	11	7	4	10	5	5	60	40	20
% SAB / clinical pregnancies	11.1	0.0	16.7	27.5	29.2	25.0	11.6	12.8	10.6	14.4	16.8	11.2
No. deliveries	8	3	5	29	17	12	76	34	42	356	198	158
% delivered	53.3	37.5	71.4	37.2	37.0	37.5	53.1	47.9	58.3	47.9	46.4	50.0
No. embryos transferred	42	24	18	230	138	92	441	217	224	2010	1171	839
Avg. no. embryos transferred	2.8	3.0	2.6	2.9	3.0	2.9	3.1	3.1	3.1	2.7	2.7	2.7
No. sacs implanted	14	4	10	62	36	26	151	68	83	648	386	262
Implantation rate	33.3	16.7	55.6	27.0	26.1	28.3	34.2	31.3	37.1	32.2	33.0	31.2

A poor pregnancy rate in donors with unexplained infertility following IVF-ET but a good success in their respective recipients would have suggested that sperm can create embryos that appear normal but do not implant. Alternatively, some occult endometrial factor could be hypothesized. Low pregnancy rates in both donors and recipients of oocytes from infertile donors would have suggested that oocytes can produce normal-appearing embryos that do not implant.

The relatively high rate of failed or low percentage fertilization rate in the donors with unexplained infertility using conventional insemination also suggests that fertilization failure may be a factor in unexplained infertility related to the sperm and not the oocyte. If the oocyte was the problem, one should have found that the recipients of oocytes from infertile donors with unexplained infertility would similarly be found to have the highest rate of low fertilization rates amongst the recipients and this was not the case. One can surmise that if exposing the oocyte to 50,000 sperm (as is done with conventional oocyte insemination) in women with unexplained infertility, results in a 12.5% failed fertilization rate and a 44% low fertilization rate, that in nature where after intercourse or intrauterine insemination, a far lower number of sperm reach the oocyte that fertilization failure may be one of the more common causes of unexplained infertility. Then based on donor-recipient comparisons, it would seem that it is the sperm, not the oocyte, that may be the main factor in failed fertilization. Therefore one reason why IVF-ET is successful despite unexplained infertility is by exposing the oocyte to a larger quantity of sperm that have a lower fertilization potential. What percentage of the cases of unexplained infertility is this mechanism operational vs other theoretical problem, e.g., sperm not reaching the oocyte, or abnormal fallopian tube formation, remains to be determined.

Though previous studies have found ICSI to provide higher fertilization rates than conventional oocyte insemination, the process of ICSI may lead to a lower pregnancy

rate [3]. Considering extra costs to the patient and increased labor time for the embryologists, these data can help a given IVF center to develop certain strategies as to which infertility etiologies to perform conventional oocyte insemination in all the oocytes and which etiologies, e.g., unexplained infertility, where ICSI on all or half of the oocytes retrieved may be more advantageous to prevent failed or low fertilization rates and thus insufficient number of embryos generated [4, 5].

This study also shows that IVF centers using infertile donors as a source of oocytes for recipients should not eliminate those with unexplained infertility. Knowledge of these data may help patients to be more open-minded about choosing a donor with unexplained infertility as opposed to male or tubal factor as their source of donor oocytes.

## References

- [1] Check J.H.: "Cryptic infertility and therapeutic options". *Clin. Exp. Obstet. Gynecol.*, 2001, 28, 205.
- [2] Check J.H., Fox F., Choe J.K., Krotec J.W., Nazari A.: "Sharing of oocytes from infertile versus paid donors results in similar pregnancy and implantation rates". *Fertil. Steril.*, 2004, 81, 703.
- [3] Check J.H., Bollendorf A., Wilson C., Summers-Chase D., Horwath D., Yuan W.: "A retrospective comparison of pregnancy outcome following conventional oocyte insemination vs intracytoplasmic sperm injection for isolated abnormalities in sperm morphology using strict criteria". *J. Androl.*, 2007, 28, 607.
- [4] Check J.H.: "Intracytoplasmic sperm injection may have disadvantages". *Fertil. Steril.*, 2008, 89, 1844.
- [5] Check J.H., Katsoff B., Summers-Chase D., Yuan W., Horwath D., Choe J.K.: "Pregnancy rates per embryo transfer (ET) may be improved by conventional oocyte insemination for male factor rather than intracytoplasmic sperm injection (ICSI)". *Clin. Exp. Obstet. Gynecol.*, 2009, 36, 212.

Address reprint requests to:  
J.H. CHECK, M.D., Ph.D.  
7447 Old York Road  
Melrose Park, PA 19027 (USA)  
e-mail: laurie@ccivf.com