

The Embryologists'

N E W S L E T T E R

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Relevance of Assisted Hatching with Blastocyst Stage Transfer

*The First Congress on Controversies In Obstetrics, Gynecology & Infertility
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Summary

When a blastocyst expands with the growth of the blastocoel, it stretches and thins the zona pellucida (ZP), ultimately rupturing the ZP allowing the embryo to hatch free ready for implantation. In the event this does not occur, then an otherwise potentially viable embryo may not implant. Assisted hatching (AH) has been developed to overcome this, but has been applied mostly to day-2/3 embryos (Cohen et al, 1992).

More recently it has been reported that total zona removal with pronase can be successfully undertaken with human blastocysts (Fong et. al., 1998), to enable "naked" fully-hatched blastocysts to be transferred to the uterus ready for immediate implantation.

By taking a less aggressive approach with acidified Tyrode's medium, it is equally possible to drill a large hole in the ZP of a blastocyst, without the risks associated with global exposure of the embryo to pronase. Initial retrospective comparison of AH applied in this manner to the "slower" day-6 blastocysts suggests a distinct benefit in terms of implantation when com-

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First Wave Results: 1999 Embryologists Newsletter Salary Survey

Stan Colquitt
Medical Market Analysts

First, let me extend our thanks to all of you who completed the 1999 Embryologists' Newsletter Annual Salary Survey. We have received 65 responses from 41 practices to the first wave of questionnaires. The responses to the second wave, contained in this issue, will cause our sample to exceed the record set in 1998 (72). We will update this survey information once the responses to the second wave are tabulated. We decided to publish the first wave results because of the numerous requests we have had for these data.

There are limitations to this type of survey information. The audience is relatively small consisting of approximately 475 practicing Embryologists/Andrologists in the United States. Most mail surveys yield a response rate of approximately 10-15%. The larger the mailing audience, the greater the number of responses which leads to greater sampling accuracy. This is why we choose to conduct two "waves" of surveys and it emphasizes the need for each of you to complete your survey.

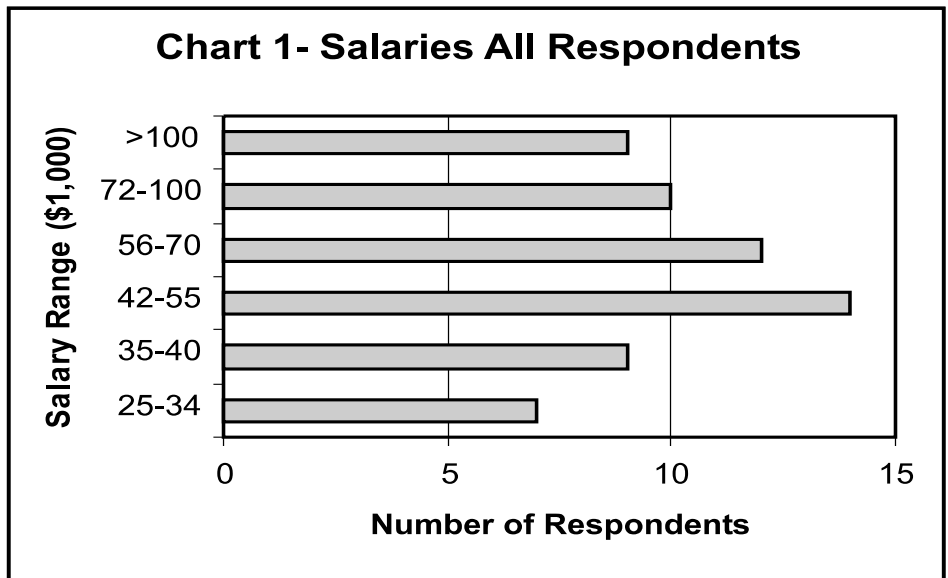
Several surveys are sometimes received from members of the same practice. A member of the embryology team notices the survey and encourages his/her colleagues to submit their copies. This can skew the results if a

particular "high responding" practice pays salaries outside of the norm. We are careful to consider this effect when analyzing the responses.

There are individuals in the embryology community who earn salaries far above, or below, the median range. This creates a large range of salaries. Dependent upon the variance of these salaries, they are sometimes removed before calculating certain statistical values. When data are removed, it is noted in the analyses.

Now that we have the qualifiers out of the way, we can discuss the findings that are valuable to you and your practice. Let me emphasize that we need everyone to complete a survey.

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pared to non-AH control blastocysts.

Introduction

Extended culture of human embryos to the blastocyst stage enables increased selection potential of embryos for transfer. This achieves improved pregnancy rates, higher implantation rates per embryo transferred allowing fewer embryos to be replaced into the uterus, thus decreasing the risk of multiple implantation (Gardner et al, 1998). Additionally, the feasibility of growth to the blastocyst stage itself can act as a diagnostic tool and as a potential passive screen for certain aneuploidies (Jones & Trounson, 1999).

In vitro culture may continue for 5 or 6 days depending on the rate of development of the embryos to the blastocyst stage. This appears very patient specific, and is probably related directly to the viability of individual embryos. AH has been shown to accelerate implantation (Liu et al, 1993), probably through earlier release of the embryo from its ZP. Hence, delayed development of day-6 blastocysts might be compensated for by use of AH.

Materials and Methods

All normal zygotes were maintained individually in micro-droplets of stage-appropriate culture medium until day-6 of development, when blastocysts were selected according to morphology and degree of expansion. An initial group of women

(n=41) had blastocysts transferred with the ZP intact on day-6 (Control Group). A subsequent group of day-6 transfer women (n=39) were offered AH prior to transfer.

In this Test Group all blastocysts were exposed to 0.1 M sucrose in modified HTF for 1 minute to shrink the embryo, and a hole (35 to 40 micrometers) was drilled with acidic Tyrode's medium in the ZP away from the shrunken embryo. After washing, such AH blastocysts were allowed to re-expand prior to embryo transfer (ET, 1 to 4 hours later).

Implantation rate (IR), clinical and ongoing pregnancy rates (CPR, OPR) were retrospectively compared after the transfer of day-6 blastocysts either with intact ZP or following ZP drilling.

Results

Table I shows the outcomes relative to each study group following ET of an average of 2.0 blastocysts in the Control Group, CPR, OPR and IR were 29%, 22% and 14% respectively. This compared with the Test Group,



Day 6 Blastocyst

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Table I

	DAY SIX		
	CONTROL	ASSISTED HATCHING	DAY FIVE CONTROL
Cases	41	39	67
Age-Years	34.5	36.1	32.2
Embryos Transferred	2.6	2.4	2.1
Clinical Preg. Rate	29%	46%	58%
Ongoing Preg. Rate	22%	38.5%	55%
Implantation Rate	14%	22.5%	32.5%

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Practice Distribution

Twenty-three states are represented in the survey. The distribution by region is 8 from the Mid Atlantic, 9 from the Midwest, 5 from the Northeast, 3 from the Northwest, 4 from the South, 7 from the Southwest, and 2 from the West. Hopefully, the second wave will generate a better response from the western states given the high number of cycles conducted in this part of the country.

Practice Volume

Respondents were asked if there practices grew, remained stable, or declined during 1999. Ninety five percent stated that their practices grew. One might expect that an increase in regional ART centers would cause a decline in volume at large ART centers that previously served greater geographic areas. This was not the case as all programs that exhibited a decline conducted ≤ 200 cycles. Twenty percent of practices are academic, 25% are hospital based, and 56% are private.

Baby boomers continue to age and one would expect cycle volume to decline as this segment passes reproductive age. Continued growth could be attributable to several factors including increased patient education and public awareness, better referral patterns, and increased marketing activities by ART programs.

Cycle Volume

The average number of IVF cycles (donor not included) conducted is 226.75 and the median is 150. The range is 50-1,200 cycles. The average number of cycles reported in 1998 was 227.9. 29.2% of practices report 100 or fewer cycles, 34.1% report 101-200, 26% from 201-500 and 9.7% above 500. When Donor Egg and Cryo cycles are included, the average number of cycles rises to 314 with a median of 246.

Eighty three percent of centers have a Donor Egg program. The average number of Donor Egg cycles is 25.8 and the median is 12. The range is from two to 250.

Ninety percent of centers have a Cryo program. The average number of cycles conducted is 65.9 and the median is 50. The range is five cycles to 350. Approximately 30% of total ART volume is due to Donor Egg or Cryo cycles.

Labor

The average number of embryologists per practice is 3.24 and the median is three. This compares to 2.86 embryologists per practice in 1998 and equates to 97.2 cycles (IVF, Donor and Cryo) per embryologist. Eighty one percent of respondents perform embryology and andrology functions. Eighteen percent do little or no andrology work.

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Respondents Profile

Sixty-six responses have been received to date. The audience consists of 24 laboratory directors who manage an average of 2.23 individuals each. 8.6% of directors have a Bachelors degree, 4.3% are Masters, 30.4% are MD's, and 56.5% are Ph.D. trained. This compares favorably to the 1998 survey in which 52% of respondents were Ph.D. trained.

Salary Analysis

The mean salary of all respondents is \$65,723, which is an increase of 13.8% from 1998. The range is \$27,000 to \$196,000, the median is \$56,000 and the standard deviation is \$33,160. There is no correlation between the number of cycles conducted and compensation.

60.6% of respondents are female and 39.3% are male. The average salary for females is \$52,521 (median \$48,100, SD \$20,084). The average salary for males is \$88,563 (median \$86,000, SD \$38,745). A similar gender gap was seen in the 1998 survey.

The mean salary for laboratory directors is \$96,491 (median \$93,500, SD \$31,463). This compares to a mean of \$47,062 (median \$43,250, SD \$14,589) for non-directors.

11.4% of respondents are Masters trained, 49.1% are Bachelors, and 39.3% are

Ph.D.s. The mean salary for Masters embryologists is \$53,657 (median \$50,000, SD \$16,530). This compares to a mean of \$50,361 in 1998.

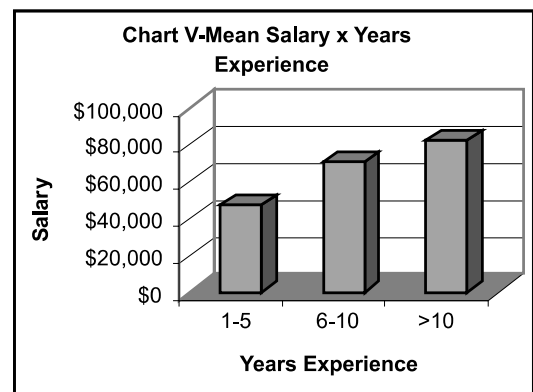
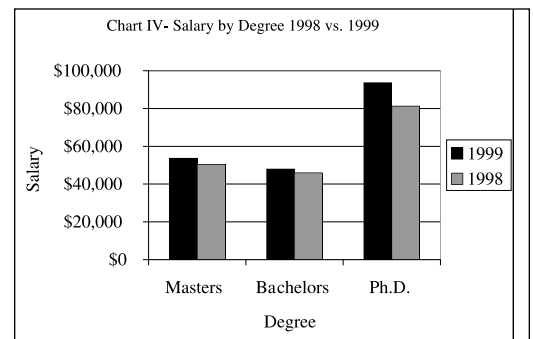
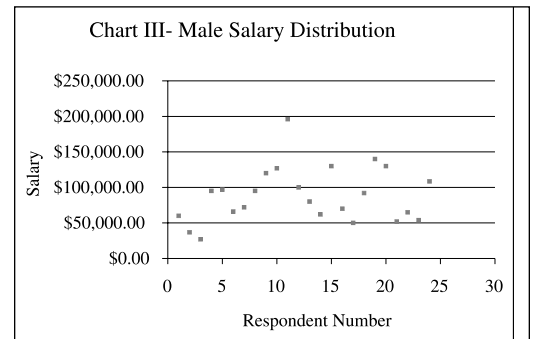
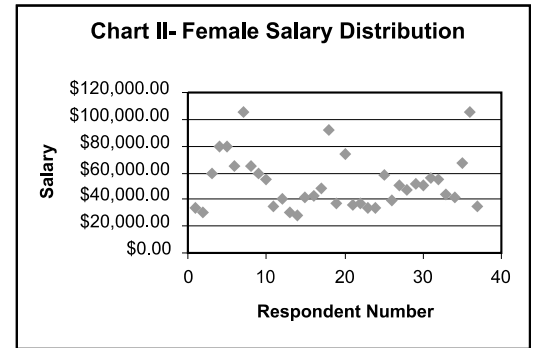
The mean salary for Bachelors trained embryologists is \$47,958 (median \$42,250, SD \$17,196) This compares to a mean of \$45,942 in 1998. The mean salary for Ph.D. trained embryologists is \$93,658 (median \$93,400, SD \$33,377). This compares to a mean of \$81,264 in 1998.

Embryologists with 1-5 years experience earn a mean salary of \$47,450 (median \$37,000, SD \$19,508). Embryologists with 6-10 years experience earn a mean salary of \$70,480 (median \$66,250, SD \$24,704) Those with >10 years experience earn a mean salary of \$82,091 (median \$65,000, SD \$38,858).

Thirty five percent of respondents receive bonus compensation, which represents a 14% increase from 1998. Ninety six percent of respondents state that they have healthcare benefits. This represents a significant increase from the 1998 survey result of 67%.

Conclusions

We will present summary conclusions based upon these data once the second wave of



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responses is received. Please complete the survey in this newsletter on page 17 or complete the online form at www.embryologists.com. If you would like us to examine additional parameters, please contact Stan Colquitt at www.embryologists.com. ■

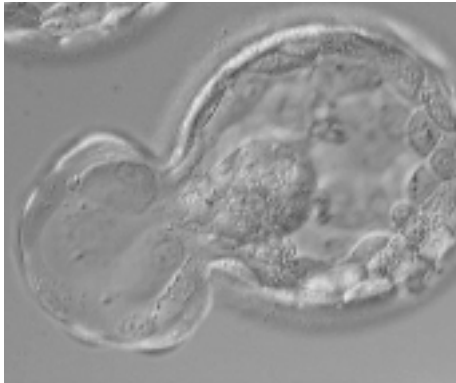
Announcement: International Blastocyst Registry

Rusty Pool, Ph.D.

I would like to invite, on behalf of Cam Jansen, MD. Ph.D., all embryologists to contribute data to the International Blastocyst Registry. This can be accomplished easily on the Internet. The address is www.rdgg.nl/blastocyst, and it can also be found at the ESHRE site (www.eshre.com) then at the 'links' session under the chapter 'infertility', and at our Web site (www.ivf.nl) then in the "English section". You only have to fill in two forms per year of entry: 'culture conditions,' and one of the three forms of the 'outcome'. They have made a deliberate decision that is not possible to enter results in terms of number of pregnancies per transfer.

As Cees said, "So far 53 centers from 23 countries have agreed to participate, in total responsible for over 3000 pregnancies from blastocysts. With this considerable body of data we will be better informed on the pro's and con's of our policy". I agree wholeheartedly and hope everyone will take a few moments to contribute data to this important endeavor. ■

Continued from Page 5



Day 6 Blastocyst Post AH

in which all blastocysts underwent AH (average 2.4 for ET), where CPR, OPR and IR were 46%, 38.5% and 22.5% respectively.

X2 analysis of these two day-6 Groups showed the following: AH Test versus Control - CPR, $p < 0.05$; OPR, $p < 0.1$; IR, $p < 0.1$. With blastocyst transfers with day 5 Controls in our program yielding CPR, OPR and IR of 58%, 55% and 32.5% respectively (significantly different from the day-6 Control Group; $p < 0.05$), clearly day-6 Control blastocysts were performing worse, even though their morphology was often comparable with blastocysts transferred on day-5.

Conclusions

Simplistically speaking, the fact that day 5 embryos seem consistently to outperform the day-6 embryos prior to the use of AH would seem to favor strongly the transfer of embryos on day 5, as if somehow the extended culture were deleterious in some way to the health of the embryo. This interpretation, however, limits the potential to maximize the selection of embryos at the blastocyst stage, in that not all embryos will have undergone blastulation by day 5.

Leaving embryos until day-6 for ET can increase the overall population of blastocysts to choose from for transfer. With AH on day-6 as a tool to enhance implantation of these "slower" embryos, it should be possible to achieve improved pregnancy rates through improved selection. The results of

this retrospective study suggest a distinct benefit from day-6 AH, with few of the concerns related to day-3 AH with premature opening of the ZP, and where rupture of blastomeres through the ZP hole may occur during traumatic ET.

The improvement of implantation seen with the day-6 AH embryos is especially noteworthy since the AH group was both an older population of women who received a slightly lower number of embryos at ET. Interestingly, after day-6 AH many blastocysts were already hatching or fully escaped from their zonae at the time of ET.

A prospective randomized study is currently being undertaken to attempt to confirm these results. Further, it is conceivable that laser drilling might further facilitate the ease with which blastocyst AH may be performed.

References

COHEN J. *Zona pellucida micromanipulation and consequences for embryonic development and implantation*. In Cohen J, Malter HE, Talansky BE & Grifo J (eds.), *Micromanipulation of Human Gametes and Eggs*, Raven Press, New York, pp. 191-209, 1992.

FONG CY, BONGSO A., NG SC, KUMAR J., TROUNSON A & RATNAM S. *Blastocyst transfer after enzymatic treatment of the zona pellucida: improving in-vitro fertilization and understanding implantation*. *Hum Reprod*, 13, 2926-32, 1998.

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GARDNER D.K., SCHOOLCRAFT W.B., WAGLEY L., SCHLENKER T., STEVENS J., & HESIA J. *A prospective randomized trial of blastocyst culture and transfer in in-vitro fertilization.* Hum Reprod 13, 3434-40, 1998.

JONES GM. & TROUNSON AO., *Blastocyst stage transfer: pitfalls and benefits. The benefits of extended culture.* Hum Reprod 14, 1405-8, 1999.

LIU HC, COHEN J. ALIKANI M., NOYES N. & ROSENWAKS Z., *Assisted hatching facilitates earlier implantation.* Fertil Steril 60, 871-5, 1993. ■

Meeting Announcement and Call for Abstracts

ART in Y2K:

Challenges and Strategies in Assisted Reproductive Technology

AUGUST 2-5, 2000

This meeting, which will be held at the King Kamehameha's Kona Beach Hotel in beautiful Kona, Hawaii, will provide assisted reproductive technology (ART) laboratory technologists, physicians, reproductive biologists, and allied health professionals an opportunity to discuss current and future challenges of our field and how to best deal with them. An internationally recognized faculty, including **Drs. Barry Behr, Patrick Quinn, Marijo Kent-First, Neal First, Paul Turek, Carol Brenner, Tetsunori Mukaida, Phil McNamee and Alan Handyside**, among others, will lead these discussions and share their knowledge and strategies for overcoming problems that occur in the ART clinic and laboratory. Topics to be discussed include:

- New developments in the culture of human embryos
- Detection of Y chromosome microdeletions, and genetic causes of male infertility
- Preparation, cryopreservation and use of testicular sperm in ART
- New developments in cryopreservation of human gametes and embryos
- Nuclear transfer, Ooplasmic transplantation, and new state-of-the-art DNA microarray technology
- Clinical management of the infertile patient

In addition to formal presentations by the faculty, **abstracts will be accepted** (June 1, 2000 deadline) for poster presentation and round table discussions are planned in the areas of clinical and laboratory ART and reproductive biology. Ample opportunity for in depth interaction between the faculty and all participants will be available and a true workshop environment will be maintained. This program will offer 1.5 CEU. Registration fee (\$250 prior to April 1, 2000) includes three lunches, breaks, reception and proceedings. Sponsored in part by SAGE Biopharma, American Association of Bioanalysts, Promega, Irvine Scientific, Biogenics, Medi-Cult, Serono, and Paradox Consultants. For more information, abstract and registration forms, visit <http://wichita.kumc.edu/users/bkeel/diveart.html>, or contact: Brooks A. Keel (bkeel@kumc.edu) or Tammie K. Schalue (tschalue@unmc.edu), Women's Research Institute, 1010 N. Kansas, Wichita, KS 67214. 316-293-1880 Fax 316-293-1881.

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