

the top 25 programs for SDR in women ≤ 37 for two consecutive years, 2005 and 2006. These 12 programs were administered a 15-page survey detailing their program's practices.

RESULTS: 10 of the 12 programs responded. Following hCG, oocyte retrieval is performed 34(10%), 34.5(10%), 35(20%), and 36(60%) hours later. One program uses a double-lumen needle exclusively, whereas 60% use the single-lumen needle exclusively. Mean suction pressure during oocyte aspiration is 110mmHg (range 80-180mmHg). 6/10 use a soft-tipped catheter only for ET and 8/10 always use ultrasound-guidance. Half the programs surveyed administer valium to all patients prior to ET whereas 2/10 never do. While all programs perform both cleavage stage and blastocyst ETs, the majority are using day 2/3 transfers (62.9% vs. 41.7%, respectively). The average number of embryos transferred in women ≤ 37 was 2.3 in 2005 and 2.2 in 2006. 50% of programs remove the ET catheter immediately after embryo expulsion whereas 50% wait (range 1-30 seconds) before immediate withdrawal. All programs supplement with progesterone during the luteal phase, but its time of discontinuation varies from pregnancy test day (20%) to 12 weeks gestational age (20%). Estrogen supplementation is utilized in all patients by 5/10 programs and in poor responders in another 3/10.

CONCLUSIONS: While ultrasound-guided ETs and luteal phase progesterone support are common practices among excellent IVF programs, many of the other techniques and protocols used following hCG administration are highly variable implying that these may not be as important compared to other aspects of an IVF cycle in determining a program's success.

O-271 Wednesday, October 21, 2009 4:30 PM

GENE EXPRESSION OF HUMAN CUMULUS CELLS AS A BIOMARKER OF HUMAN EMBRYO POTENTIAL AND PREGNANCY OUTCOME: A PROSPECTIVE STUDY. G. Ouandaogo, S. Assou, D. Haouzi, H. Dechaud, J. De Vos, S. Hamamah. CHU Montpellier, Institute for Research in Biotherapy, INSERM U847, Montpellier, France; Université Montpellier I, Montpellier, France; Unité biologie Clinique d'AMP - DPI, Montpellier, France.

OBJECTIVE: The pregnancy and live birth rates following intra cytoplasmic sperm injection (ICSI) and *in vitro* fertilization (IVF) attempts remain low. Subjective morphological parameters are still a primary criterion to select healthy embryos used for IVF and ICSI programs. However, such criteria do not truly predict the embryo competence. The aim of this study was to evaluate the interest genes expressed in cumulus cells surrounding the oocyte used as biomarkers, to identify the a competent embryo and pregnancy outcome.

DESIGN: Human cumulus cells were analyzed by microarrays and confirmed by q-RT PCR.

MATERIALS AND METHODS: Cumulus cells from single oocyte provided from normal responder patients (n=43) referred for ICSI for male infertility were analyzed using the Affymetrix Human U133 Plus 2.0 oligonucleotide microarray. All results were confirmed by q-RT PCR. Gene expression profiles of CC (n=152) surrounding the oocyte were compared according to morphological grade of embryos and pregnancy outcome.

RESULTS: We observed that cumulus cells issued from oocytes that developed into embryos with a good morphology (grade 1-2) and/or associated with ongoing pregnancy had differing gene expression profile. Among of candidate list genes, BCL2L11 (x6.9, $p < 0.001$), PCK1 (x3.4, $p = 0.001$) and NFIB (x0.3, $p < 0.001$) are significantly expressed in cumulus cells and correlated with embryo potential and successful pregnancy.

CONCLUSIONS: The gene expression profiling of human cumulus cells correlates with embryo potential and pregnancy outcome. Our results demonstrate a differential gene expression between human cumulus cells from oocytes resulting in different pregnancy outcome. BCL2L11, PCK1 and NFIB genes can be used as biomarkers to identify a competent embryo and predicting pregnancy. This analysis is a novel concept, offering a new potential strategy for competent embryo selection.

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O-272 Wednesday, October 21, 2009 4:45 PM

GONADOTROPIN STIMULATION OVER 12 DAYS IN IVF IS A NEGATIVE PREDICTOR OF LIVEBIRTH: MULTIVARIABLE ANALYSIS OF 699 CYCLES. M. Chuang, A. Zapantis, M. Taylor, S. K. Jindal, H. J. Lieman, A. J. Polotsky. Obstetrics & Gynecology and Women's Health, Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: The impact of modifiable factors on ART success, such as gonadotropin stimulation, is not well understood. The objective was to determine if the duration of stimulation predicts live birth after ART.

DESIGN: Retrospective.

MATERIALS AND METHODS: All 794 IVF or ICSI cycles using fresh autologous oocytes between 1/2004-12/2007 were analyzed. In addition to bivariate analyses, multivariable logistic regression was done to determine predictors of live birth and clinical pregnancy with duration of stimulation as an independent variable of interest.

RESULTS: 699 cycles resulted in egg retrieval (88%). The highest tertile of duration of gonadotropin stimulation was associated with significantly lower pregnancy rates.

TABLE. Study characteristics by duration of gonadotropin stimulation

	<10 days, n=100	10-12 days, n=439	>12 days, n=160	P
Age, yrs	34.6 (4.5)	35.5 (4.3)	34.5 (4.2)	0.02
FSH, mIU/ml	7.6 (2.7)	7.7 (2.5)	8.0 (3.0)	0.48
Primary infertility, %	40.0	41.2	51.3	0.07
BMI, kg/m ²	26.2 (6.3)	25.4 (5.5)	26.1 (6.0)	0.39
Total dose of gonadotropins, IU	2401 (1188)	3031 (1581)	4319 (2065)	<0.01
Oocytes retrieved	11.3 (6.3)	12.8 (7.1)	11.7 (6.6)	0.06
Embryos transferred	2.6 (1)	2.6 (0.9)	2.5 (0.9)	0.59
Day 5 transfer, %	2.0	9.3	6.9	0.04
Clinical pregnancy, %	36.0	37.8	24.4	<0.01
Live Birth, %	30.0	30.3	18.8	0.02

Data presented as mean (s.d.) unless otherwise indicated

Multivariable analysis indicated that duration of stimulation of >12 days decreased the likelihood of live birth by 44% (OR 0.56, 95% CI: 0.34-0.93) after adjustment for age, FSH, total dose of gonadotropin received, oocytes retrieved & embryos transferred. Excluding 8 coasted patients from the cohort did not significantly alter the results.

CONCLUSIONS: Prolonged duration of gonadotropin stimulation is an independent negative predictor of ART success.

O-273 Wednesday, October 21, 2009 5:00 PM

WORLDWIDE DIFFERENCES IN ACCESS TO ASSISTED REPRODUCTION TECHNOLOGY (ART) INFLUENCE PROVIDERS/ CONSUMERS DECISIONS ON THE NUMBER OF EMBRYOS TRANSFERRED, AFFECTING THE PROPORTION OF MULTIPLE BIRTHS. F. Zegers-Hochschild, D. G. Adamson, K. G. Nygren, J. de Mouzon, O. Ishihara. Unit of Reproductive Medicine, Clinica las Condes, Santiago, RM, Chile; Fertility Physicians of Northern California, Palo Alto, CA; IVF Units, Sophiahemmet Hospital, Stockholm, Sweden; INSERM U822, Hôpital de Bicêtre, Paris, France; Department of Obstetrics and Gynecology, Saitama Medical University Hospital, Moroyama, Saitama, Japan.

OBJECTIVE: Economic factors influence how risks and benefits are weighed among providers and consumers of ART treatments. This report demonstrates that free access to ART as opposed to out of pocket funding, influence the number of embryos transferred, delivery rates and high order multiple births as well as the type of treatment.

DESIGN: Retrospective analysis of 2004 world data.

MATERIALS AND METHODS: Availability is expressed as the number of initiated cycles per million inhabitants or by calculating the number of infertile women theoretically requiring ART. This data is correlated with the proportion of 1, 2, 3 and ≥ 4 embryos transferred; delivery rates by transfer; and the proportion of singletons, twins and \geq triplets. Numerical data was obtained from procedures reported to the International Committee Monitoring ART (ICMART).

RESULTS: In countries with free access to ART, the proportion of initiated cycles varied between 2008/million inhabitants in Denmark to 1062 in France. In countries with no reimbursement, the proportion of ART treatments drops to 26 to 200/million in Latin America and some European countries without reimbursement. The US performs only 357 cycles/million. Conversely, the proportion of 3 and 4 embryos transferred increases from 5 to 9% in Nordic countries to 20 to 40% in southern Europe, 52% in the US and a mean of 60% in Latin America. Consequently, the proportion of multiples/high order births is 33%/6% in Latin America, 32%/1.1% in the US and

approximately 15%/0.3% in Denmark, Belgium, and Sweden. Similarly, there is a higher proportion of ICSI (76-80%) performed in countries with limited access to ART.

CONCLUSIONS: Social and economic factors influence reproductive decisions. The risks involved in multiple gestations can be minimized if the costs of childbearing are covered by society as a whole. When individuals fund infertility treatment, the desire to conceive has greater influence than the risks of multiple births.

O-274 Wednesday, October 21, 2009 5:15 PM

RANDOMIZED CONTROLLED TRIAL EVALUATING THE EFFECT OF A GnRH-ANTAGONIST IN WOMEN WITH PCOS UNDERGOING OVULATION INDUCTION WITH GONADOTROPINS AND INTRAUTERINE INSEMINATION (IUI): INTERIM ANALYSIS. L. Stadtmayer, H. Beydoun, S. Bocca, B. Pultz, S. Oehninger. Jones Institute for Reproductive Medicine, Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To evaluate the outcome of GnRH antagonist treatment in gonadotropin-stimulated PCOS patients undergoing IUI.

DESIGN: Prospective randomized controlled trial.

MATERIALS AND METHODS: Anovulatory PCOS women undergoing ovulation induction cycles (n=143) with IUI (TMS > 5 million) were randomized into 3 Groups. Group 1: rec-FSH alone; Group 2: rec-FSH with GnRH-antagonist initiated when follicular size reached 13 mm in diameter; Group 3: rec-FSH with GnRH-antagonist given from day 1 of stimulation. The primary outcome measure was the clinical pregnancy rate (PR) per cycle initiated. Secondary outcome measures included the total gonadotropin dose per cycle, length of treatment, serum progesterone, LH and estradiol levels on day of hCG administration, premature luteinization rate and live birth rate per completed cycle. Power analysis showed 50 cycles per group were needed to demonstrate a 25% difference in PR at a significance level of $\alpha = .05$ and $\beta = 0.20$.

RESULTS: The clinical PR/cycle initiated and live birth rates per cycle completed in patients in Group 2, were higher (17/49,34%, 15/46,32%), compared with Groups 1 (11/50, 22%, 9/47,19%) or Group 3 (10/44,23%, 7/37,19%), P=0.09. All except 2 pregnancies were singletons (2 twins in Group 2). In the absence of antagonist (Group 1), premature luteinization occurred more often (20% vs. 0% vs. 2.% P<0.05).

TABLE 1

	Group 1	Group 2	Group 3	P
# cycles	50	49	44	
Age	30±4	31±4	30.5±4	P=0.1
r-FSH (IU)	1251±733	1313±972	1325±606	P=0.6
peak estradiol(pg/mL)	759±616	699±788	659±675	P=0.7
Peak LH IU/L	10.4±8.6	3.1±2.5	3.2±6.7	P=0.001
follicles>16	2±1.5	2.4±1.8	2.2±1.9	P=0.5

t-test mean ± SD

CONCLUSIONS: Interim results show a clear trend for improved primary outcome in the flexible antagonist group. Premature luteinization occurred commonly in women with PCOS using rec-FSH alone and inhibition of LH may be the mechanism for the beneficial effect seen in Group 2.

Supported by: Organon-Schering Plough- Ganirelix® and Follistim® 600 IU per cycle.

O-275 Wednesday, October 21, 2009 5:30 PM

DAY 3 FSH LEVELS ARE NOT CORRELATED WITH THE PREVALENCE OF EMBRYONIC ANEUPLOIDY IN EMBRYOS TRANSFERRED TO PATIENTS OR CRYOPRESERVED FOLLOWING IVF. N.-A. Gueye, P. Schultz, A. Azim, N. Treff, K. Miller, R. Scott. Obstetrics Gynecology and Reproductive Science, UMDNJ-Robert Wood Johnson Medical School, Morristown, NJ; Reproductive Medicine Associates of New Jersey, Morristown, NJ.

OBJECTIVE: To determine the relationship between basal day 3 FSH levels and the prevalence of aneuploidy in embryos developing in vitro.

DESIGN: Prospective observational

MATERIALS AND METHODS: One hundred fifty one patients undergoing 24 chromosome microarray based aneuploidy screening as a component of their IVF cycle were studied. Microarray PGD results were available on 1000 embryos from these patients. These patients had all undergone ovarian reserve testing in the same core laboratory within the clinical program. The highest prior FSH level was determined for each patient at the time they underwent their IVF cycle. This number was compared to the prevalence of aneuploidy in the embryos which were of suitable quality to either be transferred or cryopreserved for future use. 24 chromosome microarray based PGD was done as previously described using an Affymetrix system.

RESULTS: Basal FSH measurement varied from 3 to 25 IU/L. The percentage of aneuploid embryos varied from 0 to 100 percent. The prevalence of aneuploidy was 42.4%. There was no significant relationship between maximum prior basal FSH measurement and the percent of embryos which were aneuploid (P=0.74). There was a significant relationship between age and the percentage of embryos were normal (P=0.01). Logistic regression was done to control for age and still there was no significant relationship between the prevalence of aneuploidy and maximum prior basal FSH level.

CONCLUSIONS: The relationship between basal FSH levels and the prevalence of aneuploidy in embryos of sufficient morphologic quality to be either transferred or cryopreserved. These data indicate that the diminution in implantation potential which occurs as FSH increase is not related to aneuploidy. The mechanism remains unknown at this time. Further evaluation of those embryos which arrest in development or which are of insufficient quality to cryopreserve is needed to fully understand this relationship.

OUTCOME PREDICTORS - LABORATORY: ART

O-276 Wednesday, October 21, 2009 3:45 PM

AMMONIA, ALANINE, GLUTAMINE, AND ALANYL-GLUTAMINE CONCENTRATION IN CULTURE MEDIUM OF HUMAN EMBRYOS. J. Stevanato, I. Lebrun, E. G. Lo Turco, A. B. Victorino, R. P. Bertolla, A. P. Cedenho. Department of Surgery, Division of Urology, Human Reproduction Section, Sao Paulo Federal University, Sao Paulo, SP, Brazil; Butantan Institute, Laboratory of Biochemistry and Biophysics, Universidade de Sao Paulo, Sao Paulo, SP, Brazil.

OBJECTIVE: Embryos are selected for transfer based on morphological quality. However, improved and more objective selection methods based on embryo metabolism are necessary. We sought out to verify the relationship between ammonia (Am), alanine (Ala), glutamine (Gln) and alanyl-glutamine (Ala-Gln) concentration in culture media and embryo quality and occurrence of pregnancy.

DESIGN: Prospective case-control study.

MATERIALS AND METHODS: Culture media from 62 ICSI embryos were collected after embryo transfer and frozen until analysis of concentration of the metabolites Am, Ala, Gln, and Ala-Gln by HPLC. Culture media incubated without embryos was used for normalization. Samples were grouped by embryo morphologic quality on days 2 and 3, homogeneity of cleavage (morphology on days 2 and/or 3 thence), use of LH during hormonal stimulation, and occurrence of pregnancy. Analysis of Am, Ala, Gln and Ala-Gln concentrations were compared using Student's T-test or ANOVA, and frequencies using Chi-square. Logistic models were constructed using female age, use of LH, embryo quality, and the measured metabolites as independent variables, occurrence of pregnancy as the dependent variable.

RESULTS: Women achieving pregnancy presented lower levels of normalized Gln (1.4±0.7 and 1.9±0.7, p=0.004) and Am (0.2±0.01 and 0.3±0.1, p=0.008) than those who did not. Higher levels normalized Ala-Gln were observed in better quality embryos on days 2 and 3, and on those who presented homogeneous evolution. Embryos from patients who received LH presented higher absolute values of Ala-Gln (334.9±95.2 and 282.9±62.4 respectively, p=0.017). In logistic regression, increasing values of Gln and Ala-Gln, and decreasing values of Ala and Am led to an increase in the odds of pregnancy.

CONCLUSIONS: We may conclude that embryos with better quality on days 2 and 3 and with homogenous cleavage are associated with higher Ala-Gln concentration in culture media, and that lower levels