d/b: c n.s.). a statistically significant difference in individual mean et grades and mean pregnancy rates/et is limited to the physicians with the lowest and the highest et-score, but these preliminary results demonstrate a trend towards a higher pregnancy rate if the individual physician's et-score is lower.

Conclusion: Further study is needed to analyse the individual components generating a physician's average et-score. Although preliminary and weakened by small study populations, these data provide encouragement towards continuing efforts to monitor, and ultimately adjust, embryo transfer techniques in an attempt to improve outcome in ivf-et without risking multiple pregnancies.

P-12

Ultrasound and hysteroscopic findings in women with a history of difficult embryo transfers. K. Marikinti, T. Mathews, J. Ball, P. Brinsden. Bourn Hall Clin, Cambridge, United Kingdom.

Objective: There are, at present, no reliable predictors or preventive solutions to the problem of difficult embryo transfers (ET). Cervical stenosis is often diagnosed subjectively and cervical dilatation is performed without consistent benefits. This study was undertaken to investigate the cervico-uterine anatomical details of women with a history of difficult ETs. The data and images are presented.

Design: Prospective, case-controlled study.

Materials/Methods: Thirty women with a history of one or more difficult ETs were compared with 30 matched controls with a history of easy ETs. Use of Allis forceps and/or stylet for their previous ETs were classified as difficult transfers and use of an inner soft catheter alone or with the outer sheath were classified as easy. Trans Vaginal Scan (TVS), followed by a mock embryo transfer (MET), and then a hysteroscopy was performed in all 60 women in the luteal phase of a natural cycle.

Results: 60 women completed the study, 30 with previous difficult ETs (Group 1) and 30 with previous easy ETs (Group 2). More hysteroscopic and ultrasound abnormalities, single or multiple, were found in Group 1 and they are summarized in the following table. An acute cervico-uterine angle was strongly associated with endometrial trauma and endocervical bleeding after METs. Presence of the cervico-uterine abnormalities was also associated with various forms of occult endometrial trauma in both groups even after easy METs.

Table 1: Summary of findings in two groups after Ultrasound, MET and Hysteroscopy

	Group 1 (n=30)	Group 2: (n=30)
Ultrasound abnormalities		
Cystic lesions around cervical canal	9	2
Abnormal echos/angle at isthmus	10	7
Fibroid at isthmus	1	1
Endocervical cyst	1	1
Endocervical polyp	0	1
TOTAL	21	12
Mock embryo transfer related trauma		
Endometrium only	3	5
-sub-endometrial hemorrhage	3	4
-perforation	0	1
Endocerivcal congestion/bleed	7	0
+endometrial grooving	5	0
+endometrial tear	2	0
Sub-endometrial hemorrhage & cervicalcongestion;	0	2
Cervical bleeding	4	1
Cervical congestion	7	6
TOTAL	21	14
Hysteroscopic abnormalities		
Acute cervico-uterine angle only	5	5
+cervical lesions	8	0
-cervical cysts	6	0
-cervical folds	2	1
Cervical synechiae	4	1
Cervical polyps/cysts	4	3
Cervical folds	2	0
TOTAL	23	10

Conclusions: Targeted scanning and hysteroscopy has shown a higher incidence of cervical and cervico-uterine angle abnormalities in women with a history of difficult ETs that had not been recognised earlier. These abnormalities were associated with internal injury, both to the endometrium and/or endocervical mucosa, following MET, even after easy mock transfers. In particular, acute flexion/deflection of the uterus was a frequent finding in difficult transfers and often resulted in bleeding from the cervix after MET. Cervical stenosis was not evident in this study and cervical dilatation was not required to introduce a 3.1 mm hysteroscope. We therefore propose that a targeted ultrasound and hysteroscopic examination should be considered first before performing cervical dilatation in women with a history of difficult ETs.

P-14

Oocyte recovery and maturity following ovulatory doses of ovidrel. Ronald Carson, Patricia McShane, Samuel Pang, Isaac Glatstein. The Reproductive Science Ctr, Waltham, MA.

Human chorionic gonadotropin (hCG) is administered routinely to women to induce final maturation of oocytes prior to follicular aspiration and isolation of oocytes for insemination in vitro. A recombinant hCG (rec-hCG) became available recently and has been used for this purpose.

Objective: To compare the efficacy of rec-hCG to preparations of human urinary hCG (u-hCG) in the isolation and insemination of oocytes in vitro.

Design: 198 treatment cycles in which the patient was administered rec-hCG (Ovidrel, Serono) between January and June of 2002 were identified and compared retrospectively to 638 age-matched treatment cycles in which the patient received u-hCG during the same period; either Profasi (Serono), Pregnyl (Organon) or Novarel (Ferring).

Methods: When follicular development was deemed to be optimal on the basis of serum estradiol concentration and ovarian ultrasound, either rec-hCG (250ug sc) or u-hCG (10,000 IU im) was administered as a single dose. Efficacy was assessed as the arithmetic difference between the number of ovarian follicles (>12mm) and the number of oocytes isolated 36 hours after hCG injection, the proportion of oocytes which underwent normal fertilization following insemination and, for cases in which cumulus cells were removed prior to intracytoplasmic injection of sperm, the proportion of oocytes at metaphase II. These values were calculated for individual treatment cycles within the rec-hCG and the u-hCG groups, respectively. The statistical significance of any difference in the mean of these values for the rec-hCG and the u-hCG groups was examined using one-way ANOVA.

Results: Neither the mean age at commencement of stimulation (rec-hCG 35.8 $\pm$ 4.1, u-hCG 35.2 $\pm$ 3.9 years, $p=0.07$) nor the interval from hCG injection to follicular aspiration (rec-hCG 36.0 $\pm$ 4.9, u-hCG 35.9 $\pm$ 3.8 hours, $p=0.803$) was different between the two groups. The mean differential between the number of oocytes isolated and the number of follicles present in each patient was not different between the rec-hCG and the u-hCG cycles (rec-hCG $+0.4$ ± 5.4, u-hCG 0.0 ± 5.0 percent, $p=0.330$). Similarly, the mean proportion of oocytes forming two pronuclei at 16-22 hours after insemination (rec-hCG 55.8 ± 23.6, u-hCG 57.9 ± 24.5 percent, $p=0.273$) and the mean proportion of oocytes at metaphase II (rec-hCG 76.5 $\pm$ 1.9, u-hCG 77.0 $\pm$ 1.0 percent, $p=0.794$) were not different between rec-hCG and u-hCG cycles.

Conclusion: Ovidrel (rec-hCG) is as effective as urinary hCG in the recovery of oocytes for insemination in vitro.

P-15

Fertility preservation using ART and embryo cryopreservation prior to chemotherapy in breast cancer patients. New and safe protocol for ovarian stimulation. Dror Meirow, Eti Maman, Betty Farber, Bella Kaufman, Jehoshua Dor. Seba Medical Ctr, Ramat Gan, Israel.

Introduction: One third of breast cancer patients are at reproductive age and 6% are younger than 35. Chemotherapy treatments for breast cancer during reproductive years will result in ovarian failure in more than 50% of patients and in about 30% of patients under the age of 35. Moreover, few precious years will pass from diagnosis until patients will be allowed to conceive. Therefore, the issue of fertility post treatment is of major concern. IVF and Embryo Cryopreservation are used to preserve fertility potential prior to chemotherapy treatments in some malignancies. However, the presence of high estrogen levels during ovarian stimulation for IVF can increase the risk and therefore is questionable in breast cancer patients.

Objectives: To find a safe and effective ovarian stimulation protocol for IVF in breast cancer patients that produces substantial number of eggs.

Material and Methods: 1. Hormonal status of 15 non-menopausal breast

cancer patients treated with Tamoxifen 20mg/day was evaluated. 2. Young patients (No.12) suffering from recently diagnosed breast cancer had IVF cycle prior to chemotherapy. Tamoxifen 20mg P.O. was added during stimulation in order to protect the breast from possible adverse effects of high E2 in addition to ovarian stimulation protocol for IVF that consisted of gonadotropins and GnRH-a. The time needed to complete the cycle, ovarian response to the combined stimulation protocol: the No. of eggs retrieved, egg's morphology and hormone levels in follicular fluid were recorded. Fertilization rate and the quality of embryos were evaluated.

Results: In the group of 15-non menopausal breast cancer patients treated with adjuvant Tamoxifen 20mg/d (mean age 41y) E2 levels were persistently elevated between 1500-10,000 pmol/L. Only with monthly Goserelin 3.6 mg treatment E2 levels dropped below 100 pmol/L. All IVF patients ended cycle prior to chemotherapy within the time frame of 4-6 weeks (accepted time from surgery to chemotherapy). Max. serum E2 levels was 5700 (1900-7900) pmol/L, the mean No. of oocytes retrieved was 10 (3-15), with good morphology of oocyte comulus complex. E2 and Progesterone levels in follicular fluid were similar to controls. Fertilization rate and morphology of embryos prior to cryopreservation in cycles where Tamoxifen was added to stimulation protocol where comparable to controls.

Conclusions: Tamoxifen is considered effective and safe adjuvant therapy for breast cancer in spite of persistent extremely high E2 levels in premenopausal patients. The proposed stimulation protocol in breast cancer patients provides protection with Tamoxifen to the breast during stimulation, and is significantly superior to any other known protocols for breast cancer patients concerning the No. of oocytes retrieved and the No of cryopreserved embryos. In contradiction to persistant extremely high E2 levels with adjuvant Tamoxifen, this stimulation protocol provides only short duration of high E2 that is protected by Tamoxifen.

P-16

The impact of assisted reproduction in the definition and incidence of unexplained infertility. Amparo Ruiz, Maria J. De los Santos, Carmina Vidal, José Remohí, Antonio Pellicer. IVI Inst Valenciano de Infertilidad, Valencia, Spain.

Objective: Unexplained infertility (UI) has been described to be present in 15% of infertile couples. Assisted Reproduction (AR) has been not only a useful tool routinely employed in the treatment of infertility, but also has provided valuable information about new causes affecting the reproductive process. As a result, the proportion of couples in which the etiology of infertility remains unknown has substantially decreased. The aim of this study was to analyze the actual incidence of UI in the era of AR.

Design: Retrospective analysis of patients undergoing intrauterine insemination (IUI), initially defined as UI due to the presence of regular menstrual cycles, normal basal serum gonadotropin levels, hysterosalpingogram, transvaginal ultrasound scan, and semen analysis. If IUI failed after 4 cycles, they were treated by IVF/ICSI. Some of the failed cases underwent oocyte donation or IUI with donor sperm). The AR techniques employed, the problems found, and the final outcome, were employed to redefine the etiology of infertility.

Materials and Methods: A total of 457 couples undergoing IUI due to UI formed the study population. One hundred-fourty one reached pregnancy, and 183 abandoned or were lost. Thus, 133 further continued other AR treatments at least until a problem was found in the couple, or pregnancy was achieved by AR.

Results: Out of 133 couples undergoing AR, the cause of infertility was found in 70 (52.6%): In 32 (45.7%), the problem was mainly the oocyte because a low response, or oocytes with abnormal morphology were found; In 21 (30.0%), there was a male defect found, either by failed fertilization, or the presence of specific defects in the sperm morphology; Finally, 17 (24.3%) cases presented abnormal embryos.

Conclusion: AR has allowed the introduction of new causes of infertility such as oocytes of abnormal morphology, diminished ovarian reserve, failed fertilization, or defective embryo development. Applied to UI, AR has been able to find a specific etiology in as much as 52.6% of cases, oocyte problems accounting for almost 50% of them. Thus, the percentage of couples with UI after being treated with AR should be reduced to one half (approximately 7%) in advising our patients.

P-17

Efficacy of day 4 embryo transfer (ET) in minimizing weekend staffing requirements. Robert J. Kiltz, Debra J. Woodhouse, Donna B. Miller, Ann Marie Sciera, Jennifer T. Corona. CNY Fertility Ctr, Syracuse, NY.

Objective: Our facility is operated by a single physician who worked 7 days a week. ET were routinely performed on day 3 or day 5, including Sundays. In an effort to minimize weekend staffing needs, we evaluated the use of day 4 ET. Few studies have proven the benefits of day 4 ET, and it is rarely performed by others. The purpose of this study is to determine the efficacy of the day 4 ET.

Design: A retrospective study in a private ART center.

Materials and Methods: All fresh donor cycles, and autologous cycles in women less than 41 years of age performed from March through November 2002 resulting in ET (n=354) were included in this study. Following ICSI, all embryos were cultured in G1.2 medium to day 3. When day 3 fell on a Sunday, patients were scheduled for day 4 or day 5 ET. For those selected for extended culture, embryos were placed to Global Medium on day 3, cultured to day 4 or day 5, and subsequently transferred. Delivered or ongoing clinical pregnancy rates (CP) were determined and compared.

Results: The summary of our findings are presented in the table below:

Table 1			
DAY ET	3	4	5
# Cycles	272	44	38
Age (mean SD)	34.6± 5.6	34.5 ± 4.6	33.8± 5.0
# Embryos ET(mean SD)	3.9 ± 1.7	3.9 ±1.5	2.6 ± 1.6
CP (%)	40.1	59.1	68.4

Conclusion: As illustrated by the data, there were no detrimental effects associated with day 4 ET. Implementation of day 4 ET is an effective method of minimizing weekend staffing requirements without compromising patient care. In order to assess if day 4 ET may be superior to day 3 ET, a prospective, randomized study should be performed.

P-18

Timing blastocyst transfer: Targeting the implantation window. Claudio Ruhlmann, Alejandro G. Martínez Sr., Guillermo Terrado Sr., Edgardo D. Rolla Sr., Antonio R. Cattaneo Sr., Roberto E. Nicholson Sr. Unidad de Fertilidad San Isidro, San Isidro, Argentina.

Success of ART procedures relies on 3 steps: controlled ovarian hyperstimulation, in vitro embryo development and embryo transfer. The optimal timing for replacement of blastocyst stage embryos still remains undefined.

Study design: Observational study.

Location: Tertiary private infertility clinic.

Objective: To correlate the importance of the moment of embryo transfer at the blastocyst stage with success rate.

Patients: One hundred and fifty eight consecutive ART cycles (70 FIV, 88 ICSI) from 127 patients were included.

Blastocyst development was attained in co-culture with Vero cells.

Embryo transfer was programmed when at least one expanding blastocyst over 50% was available.

Cycles were divided in 3 groups according with the lapse between insemination and embryo replacement, group 1: less than 127 hours (n = 42), group 2: between 127-138 hours (n = 66), and, group 3: more than 138 hours (n = 50) of embryo culture.

Kruscall-Wallis and Fisher's Exact tests were applied as appropriate for statistical analysis.

Results: Clinical pregnancy rate (50%, 29% and 20%, respectively), implantation rate (27%, 15% and 10%, respectively), and, evolutive pregnancy rate (43%, 21% and 18%, respectively) were significantly higher in group 1, even when significantly less blastocysts where transferred in this group.

Conclusion: According to our study the best results are obtained with the transfer of blastocyst stage embryos <126 hours of culture after insemination. The present findings may reflect a better synchronization with the endometrial implantation window or the transfer of faster developing embryos in the group with earlier transfer.