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Current Awareness Bulletin – Fertility
February and March 2015

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Guidelines

National Institute for Health and Care Excellence (NICE)

Hysteroscopic metroplasty of a uterine septum for primary infertility
NICE interventional procedure (IPG509)

Hysteroscopic metroplasty of a uterine septum for recurrent miscarriage
NICE interventional procedure (IPG510)

Cochrane Systematic Reviews

New Reviews – February 2015

Time-lapse systems for embryo incubation and assessment in assisted reproduction

Updated Reviews – February 2015

Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities

Nitric oxide donors for cervical ripening in first-trimester surgical abortion

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Reproductive Biology & Endocrinology Online Journal
Available in fulltext from Reproductive Biology and Endocrinology at ProQuest

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Journal Articles:

1. An overview of the available methods for morphological scoring of pre-Implantation embryos in in vitro fertilization

Citation: Cell Journal, December 2015, vol./is. 16/4(392-405), 2228-5806;2228-5814 (01 Dec 2015)

Author(s): Nasiri N., Eftekhari-Yazdi P.

Language: English
Abstract: Assessment of embryo quality in order to choose the embryos that most likely result in pregnancy is the critical goal in assisted reproductive technologies (ART). The current trend in human in vitro fertilization/embryo transfer (IVF/ET) protocols is to decrease the rate of multiple pregnancies after multiple embryo transfer with maintaining the pregnancy rate at admissible levels (according to laboratory standards). Assessment of morphological feathers as a reliable non-invasive method that provides valuable information in prediction of IVF/intra cytoplasmic sperm injection (ICSI) outcome has been frequently proposed in recent years. This article describes the current status of morphological embryo evaluation at different pre-implantation stages.

Publication type: Journal: Review
Source: EMBASE
Full text: Available ProQuest at Cell Journal

2. Art and uterine pathology: How relevant is the maternal side for implantation?
Citation: Human Reproduction Update, January 2015, vol./is. 21/1(13-38), 1355-4786;1460-2369 (01 Jan 2015)
Author(s): Galliano D., Bellver J., Diaz-Garcia C., Simon C., Pellicer A.
Language: English
Abstract: Background: Assisted reproduction technology (ART) has become a standard treatment for infertile couples. Increased success rates obtained over the years have resulted primarily from improved embryo quality, but implantation rates still remain lower than expected. The uterus, an important player in implantation, has been frequently neglected. While a number of uterine pathologies have been associated with decreased natural fertility, less information exists regarding the impact of these pathologies in ART. This report reviews the evidence to help clinicians advise ART patients. Methods: An electronic search of Pub Med and EMBASE was performed to identify articles in the English, French or Spanish language published until May 2014 which addressed uterine pathology and ART. Data from natural conception were used only in the absence of data from ART. Studies were classified in decreasing categories: RCTs, prospective controlled trials, prospective non-controlled trials, retrospective studies and experimental studies. Studies included in lower categories were only used if insufficient evidence was available. Pooled data were obtained from systematic reviews with meta-analyses when available. The summary of the evidence for the different outcomes and the degree of the recommendation for interventions were based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) statement recommendations. Results: There is strong evidence that surrogacy is effective for uterine agenesis. For the remaining pathologies, however, there is very little evidence that the established treatments improve outcomes, or that these pathologies have a negative effect on ART. In the presence of an apparently normal uterus, assessing endometrial receptivity (ER) is the goal; however diagnostic tests are still under development. Conclusions: The real effect of different uterine/endometrial integrity pathologies on ART is not known. Moreover, currently proposed treatments are not based on solid evidence, and little can be done to assess ER in normal or abnormal conditions. No strong recommendations can be given based on the published experience, bringing an urgent need for well-designed studies. In this context, we propose algorithms to study the uterus in ART.
Publication type: Journal: Article
Source: EMBASE

3. Cervical conization doubles the risk of preterm and very preterm birth in assisted reproductive technology twin pregnancies
Citation: Human Reproduction, January 2015, vol./is. 30/1(197-204), 0268-1161;1460-2350 (01 Jan 2015)
Author(s): Pinborg A., Ortoft G., Loft A., Rasmussen S.C., Ingerslev H.J.
Language: English
Abstract: STUDY QUESTION Does cervical conization add an additional risk of preterm birth (PTB) in assisted reproduction technology (ART) singleton and twin pregnancies? SUMMARY ANSWER Cervical conization doubles the risk of preterm and very PTB in ART twin pregnancies. WHAT IS KNOWN ALREADY ART and cervical conization are both risk factors for PTB. STUDY DESIGN, SIZE, DURATION In this national population-based controlled cohort study, we included all ART singletons and twin deliveries from 1995 to 2009 in Denmark by cross-linkage of maternal and child data from the National IVF register and the Medical Birth register. Furthermore, control groups of naturally conceived (NC) singletons and twins were extracted. Cervical diagnoses were obtained from the Danish Pathology register. Cervical conization included both cold knife cone and LEEP (loop electrosurgical excision procedure) but not cervical biopsies. The main outcomes measures were PTB (PTB < 37 + 0 gestational weeks), very preterm birth (VPTB < 32 + 0 gestational weeks) and preterm premature rupture of membranes (PPROM). PARTICIPANTS/MATERIALS, SETTING, METHODS In all 16 923 ART singletons and 4829 ART twin deliveries were included. A random sample of NC singletons, 2-fold the size of the ART singleton group matched by date and year of birth (n = 33 835) and all NC twin deliveries (n =
Currently, no evidence exists that any single regimen or adjuvant substance results in superior outcomes in cryopreserved embryos. The objective of this article was to review and synthesize information from the scientific literature pertaining to the preparation of endometrium for cryopreserved embryo transfer. This article is a critical review of selected scientific literature, synthesis, and formulation of opinion. Estrogen and progesterone are necessary and sufficient to induce endometrial receptivity in cryopreserved embryo transfer cycles. A variety of regimens have been described, including natural cycles using endogenous ovarian hormones and artificial or programmed cycles with exogenously administered steroid hormones. To achieve optimal synchrony between embryo and endometrium, the timing of progesterone administration needs to be adjusted to the developmental stage of the thawed embryos. There is currently no evidence that any single regimen or adjuvant substance results in superior outcomes in cryopreserved embryos. The proposed benefits of time-lapse monitoring have been implemented in many clinics worldwide. The review of the scientific literature and the synthesis of opinion indicates that time-lapse monitoring is a promising technique for improving the success of cryopreserved embryo transfer cycles. This review aims to perform a balanced discussion of the evidence for time-lapse monitoring in routine clinical settings. This review is therefore to perform a balanced discussion of the evidence for time-lapse monitoring.
embryo transfer cycles, although timing of progesterone administration does matter. Although no single regimen of endometrial preparation for cryopreserved embryo transfer has been proven superior to the others, the relative convenience and ease of use do vary, depending on the route of administration chosen and any adjuvant added to the cycle. Copyright Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

**Publication type:** Journal Article

**Source:** MEDLINE

6. **Effect of salpingectomy on ovarian reserve: A systematic review and meta-analysis**

**Citation:** Fertility and Sterility, February 2015, vol./is. 103/2 SUPPL. 1(e14-e15), 0015-0282 (February 2015)

**Author(s):** Boots C.E., Seidler E.A., Ainsworth A., Hardi A., Jungheim E.S.

**Language:** English

**Abstract:** BACKGROUND: As a treatment for ectopic pregnancy or for excision of hydrosalpinx, salpingectomy is a relatively common procedure performed on patients undergoing assisted reproductive technology (ART). However, shared vasculature in the mesosalpinx raises the question of ovarian devitalization at time of surgery. The effect of salpingectomy on ovarian reserve is not well understood and presents a unique concern in women with already diminished reserve. OBJECTIVE: The objective of this study is to ascertain the impact of salpingectomy on the future fertility of women undergoing ART by evaluating ovarian reserve and ovarian responsiveness in the ART cycle following unilateral or bilateral salpingectomy for the treatment of ectopic pregnancy or hydrosalpinx. METHODS: A systematic review was performed by searching Pub Med, Embase, Scopus, and CENTRAL for studies that compared markers of ovarian reserve and measures of ovarian responsiveness during ART before and after salpingectomy for the treatment of ectopic pregnancy or hydrosalpinx. With IRB approval, primary data from our institution was pooled in the final analysis. Meta-analysis of the data was performed using a Der Simonion-Laird random effects model. Results are reported as weighted mean difference and 95% confidence interval. RESULTS: Eight studies and our center's primary data were included, totaling 274 women. No differences were noted comparing pre-salpingectomy IVF cycles to post-salpingectomy cycles in regards to ovarian reserve parameters or ovarian response as assessed by stimulation duration, total dose of gonadotropins or peak estradiol levels. In addition, there were no differences in oocytes retrieved (Figure 1). A post-hoc power analysis determined that a study of this size would be able to detect an 8.3% difference in oocytes retrieved (1 oocyte) with 80% power. CONCLUSIONS: Our findings support the continued use of salpingectomy in the management of ectopic pregnancy and hydrosalpinges. Primary data is needed to stratify the analysis to determine if women of advanced age or diminished ovarian reserve are at a higher risk of effects from salpingectomy. (Figure Presented).

**Publication type:** Journal: Conference Abstract

**Source:** EMBASE

7. **Effect of sperm storage and selection techniques on sperm parameters**

**Citation:** Systems Biology in Reproductive Medicine, January 2015, vol./is. 61/1(1-12), 1939-6368;1939-6376 (01 Jan 2015)

**Author(s):** Sharma R., Kattoor A.J., Ghulmiyyah J., Agarwal A.

**Language:** English

**Abstract:** Sperm cryopreservation preserves the fertility of cancer patients undergoing chemotherapy, ensures sperm are available at the time of oocyte retrieval in assisted reproductive technology (ART) procedures and avoids the need for repeated sperm extraction surgeries in azoospermic patients. Conventional methods of cryopreservation involve storage in liquid nitrogen (LN2), which causes a significant decline in sperm parameters such as motility and viability and results in DNA damage. Newer methods of sperm cryopreservation such as the LN2 vapor method, vitrification, and experimental methods such as lyophilization, have significant advantages over the conventional methods in terms of cost effectiveness and ease of use. Density gradient centrifugation (DGC), swim up, and magnetic assisted cell sorting (MACS) can be used prior to or post-cryopreservation to improve post-thaw sperm quality. Cryopreservation in special carriers such as cryoloops and empty zona prevents the loss of small numbers of sperm during cryopreservation. This article will discuss these sperm preservation and selection techniques.

**Publication type:** Journal: Review

**Source:** EMBASE

8. **Efficacy of psychosocial interventions for psychological and pregnancy outcomes in infertile women and men: A systematic review and meta-analysis**

**Citation:** BMJ Open, 2015, vol./is. 5/1, 2044-6055 (2015)
9. Endometriosis may be associated with mitochondrial dysfunction in cumulus cells from subjects undergoing in vitro fertilization-intracytoplasmic sperm injection, as reflected by decreased adenosine triphosphate production

Citation: Fertility and Sterility, February 2015, vol./is. 103/2(347-352.e1), 0015-0282;1556-5653 (01 Feb 2015)
Author(s): Hsu A.L., Townsend P.M., Oehninger S., Castora F.J.
Language: English
Abstract: To determine whether endometriosis is associated with mitochondrial dysfunction in cumulus (granulosa [GC]) cells of subjects undergoing IVF-intracytoplasmic sperm injection (ICSI). Design Prospective cohort study. Setting An IVF clinic in a tertiary academic care center. Patient(s) Eleven women with endometriosis and 39 controls. Intervention(s) None. Main Outcome Measure(s) Cumulus cell adenosine triphosphate (ATP) levels, mitochondrial DNA (mtDNA), and genomic DNA (gDNA) number. Result(s) Cumulus cell ATP content was 65% lower in subjects with surgically proven endometriosis (median 312.5 attomoles/ng total DNA, interquartile range = 116.0-667.8) compared with controls (median 892.4 attomoles/ng total DNA, interquartile range = 403.0-1,412.2). There was no significant difference in mtDNA:gDNA ratio. There were no significant differences in age, body mass index (BMI), basal serum FSH level, total oocyte number, metaphase II (M2) oocyte number, metaphase I oocyte number, percentage of M2 oocytes, fertilization rate, implantation rate, or pregnancy rate (PR). Multivariate regression analysis showed significant positive correlations between ATP and [1] M2 oocyte number (r = 0.307) and [2] pregnancy (r = 0.332). There were also trends toward positive correlations between ATP and [3] age (r = 0.283), [4] total number of oocytes (r = 0.271), [5] percentage of M2 oocytes (r = 0.249), and [6] implantation rate (r = 0.293). There were no statistically significant correlations between mtDNA:gDNA ratio and any demographic factors or clinical outcomes measured. Conclusion(s) Surgically confirmed endometriosis may be associated with cumulus cell mitochondrial dysfunction in subjects undergoing IVF-ICSI for infertility, as reflected by decreased ATP production.

Publication type: Journal: Conference Paper
Source: EMBASE

Abstract: STUDY QUESTION: What is the proper way of assessing the effect of progesterone elevation (PE) on the day of hCG on live birth in women undergoing fresh embryo transfer after in vitro fertilization (IVF) using GnRH analogues and gonadotrophins? SUMMARY ANSWER: This study indicates that a multivariable approach, where the effect of the most important confounders is controlled for, can lead to markedly different results regarding the association between PE on the day of hCG and live birth rates after IVF when compared with the bivariate analysis that has been typically used in the relevant literature up to date. WHAT IS KNOWN ALREADY: PE on the day of hCG is associated with decreased pregnancy rates in fresh IVF cycles. Evidence for this comes from observational studies that mostly failed to control for potential confounders. STUDY DESIGN, SIZE, DURATION: This is a retrospective analysis of a cohort of fresh IVF/intracytoplasmic sperm injection cycles (n = 3296) performed in a single IVF centre during the period 2001-2013. PARTICIPANTS/MATERIALS, SETTING, METHODS: Patients in whom ovarian stimulation was performed with gonadotrophins and GnRH analogues. Natural cycles and cycles where stimulation involved the administration of clomiphene were excluded. In order to reflect routine clinical practice, no other exclusion criteria were imposed on this dataset. The primary outcome measure for this study was live birth defined as the delivery of a live infant after 24 weeks of gestation. We compared the association between PE on the day of hCG (defined as P > 1.5 ng/ml) and live birth rates calculated by simple bivariate analyses with that derived from multivariable logistic regression. The multivariable analysis controlled for female age, number of oocytes retrieved, number of embryos transferred, developmental stage of embryos at transfer (cleavage versus blastocyst), whether at least one good-quality embryo was transferred, the woman's body mass index, the total dose of FSH administered during ovarian stimulation and the type of GnRH analogues used (agonists versus antagonists) during ovarian stimulation. In addition, an interaction analysis was performed in order to assess whether the ovarian response (<6, 6-18, >18 oocytes) has a moderating effect on the association of PE on the day of hCG with live birth rates after IVF. MAIN RESULTS AND THE ROLE OF CHANCE: Live birth rates were not significantly different between cycles with and those without PE when a bivariate analysis was performed [odds ratio (OR): 0.78, 95% confidence interval (CI): 0.56-1.09]. However, when a multivariable analysis was performed, controlling for the effect of the aforementioned confounders, live birth rates (OR: 0.68, 95% CI: 0.48-0.97) were significantly decreased in the group with PE on the day of hCG. The number of oocytes retrieved was the most potent confounder, causing a 29.4% reduction in the OR for live birth between the two groups compared. Furthermore, a moderating effect of ovarian response on the association between PE and live birth rates was not supported in the present analysis since no interaction was detected between PE and the type of ovarian response (<6, 6-18, >18 oocytes). LIMITATIONS, REASONS FOR CAUTION: This is a retrospective analysis of data collected during a 12-year period, and although the effect of the most important confounders was controlled for in the multivariable analysis, the presence of residual bias cannot be excluded. WIDER IMPLICATIONS OF THE FINDINGS: This study highlights the need for a multivariable approach when researchers or clinicians aim to evaluate the impact of PE on pregnancy rates in their own clinical setting. Failure to do so might explain why many past studies have failed to identify the detrimental effect of PE in fresh IVF cycles. STUDY FUNDING/COMPETING INTERESTS: None. Copyright © 2015 Venetis CA, Kolibianakis EM, Bosdou JK, Lainas GT, Sfontouris IA, Tarlatzis BC, Lainas TG. Human Reproduction, 2015.
miscarriage rate. A total of 11 articles were included in the present analysis, with variable numbers of studies assessing each outcome measure. Results of statistical analyses indicated that progesterone plus estrogen treatment was more likely to result in clinical pregnancy than progesterone alone (pooled odds ratio 1.617, 95% confidence interval 1.059-2.471; P = 0.026). No significant difference between the 2 treatment regimens was found for the other outcome measures. Progesterone plus estrogen for luteal phase support is associated with a higher clinical pregnancy rate than progesterone alone in women undergoing IVF, but other outcomes such as ongoing pregnancy rate, fertilization rate, implantation rate, and miscarriage rate are the same for both treatments.

**Publication type:** Journal Article  
**Source:** MEDLINE  
**Full text:** Available *Medicine* at [Medicine](https://wwwmedicine.com)

### 12. Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities.

**Citation:** Cochrane Database of Systematic Reviews, 2015, vol./is. 2/(CD009461), 1361-6137;1469-493X (2015)  
**Author(s):** Bosteels J, Kasius J, Weyers S, Broekmans FJ, Mol BW, D’Hooghe TM  
**Language:** English  
**Abstract:** BACKGROUND: Observational studies suggest higher pregnancy rates after the hysteroscopic removal of endometrial polyps, submucous fibroids, uterine septum or intrauterine adhesions, which are detectable in 10% to 15% of women seeking treatment for subfertility. OBJECTIVES: To assess the effects of the hysteroscopic removal of endometrial polyps, submucous fibroids, uterine septum or intrauterine adhesions suspected on ultrasound, hysterosalpingography, diagnostic hysteroscopy or any combination of these methods in women with otherwise unexplained subfertility or prior to intrauterine insemination (IUI), in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).  
**SEARCH METHODS:** We searched the Cochrane Menstrual Disorders and Subfertility Specialised Register (8 September 2014), the Cochrane Central Register of Controlled Trials (The Cochrane Library 2014, Issue 9), MEDLINE (1950 to 12 October 2014), EMBASE (inception to 12 October 2014), CINAHL (inception to 11 October 2014) and other electronic sources of trials including trial registers, sources of unpublished literature and reference lists. We handsearched the American Society for Reproductive Medicine (ASRM) conference abstracts and proceedings (from January 2013 to October 2014) and we contacted experts in the field.  
**SELECTION CRITERIA:** Randomised comparisons between operative hysteroscopy versus control in women with otherwise unexplained subfertility or undergoing IUI, IVF or ICSI and suspected major uterine cavity abnormalities diagnosed by ultrasonography, saline infusion/gel instillation sonography, hysterosalpingography, diagnostic hysteroscopy or any combination of these methods. Primary outcomes were live birth and hysteroscopy complications. Secondary outcomes were pregnancy and miscarriage.  
**DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed studies for inclusion and risk of bias, and extracted data. We contacted study authors for additional information.  
**MAIN RESULTS:** We retrieved 12 randomised trials possibly addressing the research questions. Only two studies (309 women) met the inclusion criteria. Neither reported the primary outcomes of live birth or procedure related complications. In women with otherwise unexplained subfertility and submucous fibroids there was no conclusive evidence of a difference between the intervention group treated with hysteroscopic myomectomy and the control group having regular fertility-oriented intercourse during 12 months for the outcome of clinical pregnancy. A large clinical benefit with hysteroscopic myomectomy cannot be excluded: if 21% of women with fibroids achieve a clinical pregnancy having timed intercourse only, the evidence suggests that 39% of women (95% CI 21% to 58%) will achieve a successful outcome following the hysteroscopic removal of the fibroids (odds ratio (OR) 2.44, 95% confidence interval (CI) 0.97 to 6.17, P = 0.06, 94 women, very low quality evidence). There is no evidence of a difference between the comparison groups for the outcome of miscarriage (OR 0.58, 95% CI 0.12 to 2.85, P = 0.50, 30 clinical pregnancies in 94 women, very low quality evidence).  
**IMPACT:** The hysteroscopic removal of polyps prior to IUI can increase the chance of a clinical pregnancy compared to simple diagnostic hysteroscopy and polyp biopsy: if 28% of women achieve a clinical pregnancy with a simple diagnostic hysteroscopy, the evidence suggests that 63% of women (95% CI 50% to 76%) will achieve a clinical pregnancy after the hysteroscopic removal of the endometrial polyps (OR 4.41, 95% CI 2.45 to 7.96, P < 0.00001, 204 women, moderate quality evidence).  
**AUTHORS’ CONCLUSIONS:** A large benefit with the hysteroscopic removal of submucous fibroids for improving the chance of clinical pregnancy in women with otherwise unexplained subfertility cannot be excluded. The hysteroscopic removal of endometrial polyps suspected on ultrasound in women prior to IUI may increase the clinical pregnancy rate. More randomised studies are needed to substantiate the effectiveness of the hysteroscopic removal of suspected endometrial polyps, submucous fibroids, uterine septum or intrauterine adhesions in women with unexplained subfertility or prior to IUI, IVF or ICSI.

**Publication type:** Journal Article  
**Source:** MEDLINE
13. Identifying patients who can improve fertility with myomectomy

**Citation:** European Journal of Obstetrics Gynecology and Reproductive Biology, February 2015, vol./is. 185/(28-32), 0301-2115;1872-7654 (01 Feb 2015)

**Author(s):** Samejima T., Koga K., Nakae H., Wada-Hiraike O., Fujimoto A., Fujii T., Osuga Y.

**Language:** English

**Abstract:** Objective To identify the characteristics of cases and fibroids that will indicate which patients should undergo myomectomy to improve fertility. Materials and methods We recruited patients (n = 101) who had undergone myomectomy to improve fertility and received follow-up care for at least six months by the hospital. Medical records were retrospectively reviewed to analyze the pregnancy rates after myomectomy and to identify clinical factors that correlate with pregnancy rates. Cumulative pregnancy rates were analyzed using the Kaplan-Meier method and the Log rank test. The patients were then divided into three groups according to the timing of the myomectomy. The analysis was performed for all patients, for patients in the post-supernovulation and/or intrauterine insemination (post-SO/IUI) group and the post-assisted reproductive technology (post-ART) group combined, and for patients in the post-ART group. Results Sixty-three pregnancies were achieved by 58 patients (57.4%) who underwent myomectomy. The mean time period between surgery and conception was 9.8 months. Most pregnancies (91.5%) were achieved within two years after surgery. Pregnancy rates were higher in patients aged less than 36 years, with no male factors, and without severe endometriosis, in comparison with patients 36 years of age or older (p < 0.05), with male factor (p < 0.05), and severe endometriosis (p < 0.05). In the analysis of the post-ART group, pregnancy rates were higher (p < 0.05) in cases where enucleation had penetrated the endometrial cavity in comparison with patients where the cavity was not penetrated; however, fibroid characteristics did not correlate with the post-myomectomy pregnancy rate in the post-SO/IUI plus post-ART group. Conclusion Post-myomectomy pregnancy rates were higher in women who did not have additional infertility factors. These results suggest that the removal of fibroids benefits especially patients who suffer from infertility of an otherwise unknown cause: surgery should be strongly recommended for these patients. Our study also shows the difficulty in identifying fibroids for removal to improve fertility. Further studies are needed to develop new diagnostic techniques for identifying patients who can improve fertility with myomectomy.

**Publication type:** Journal: Article

**Source:** EMBASE


**Citation:** Gynecological Endocrinology, January 2015, vol./is. 31/1(7-13), 0951-3590;1473-0766 (2015 Jan)

**Author(s):** Frutos V, Gonzalez-Comadran M, Sola I, Jacquemin B, Carreras R, Checa Vizcaino MA

**Language:** English

**Abstract:** Air pollution has gained considerable interest because of the multiple adverse effects reported on human health, although its impact on fertility remains unclear. A systematic search was performed to evaluate the impact of air pollutants on fertility. Controlled trials and observational studies assessing animal model and epidemiological model were included. Occupational exposure and semen quality studies were not considered. Outcomes of interest included live birth, miscarriage, clinical pregnancy, implantation, and embryo quality. Ten studies were included and divided into two groups: animal studies and human epidemiological studies including the general population as well as women undergoing in vitro fertilization and embryo transfer (IVF/ET). Results from this systematic review suggest a significant impact of air pollution on miscarriage and clinical pregnancy rates in the general population, whereas among subfertile patients certain air pollutants seem to exert a greater impact on fertility outcomes, including miscarriage and live birth rates. Besides, studies in mammals observed a clear detrimental effect on fertility outcomes associated to air pollutants at high concentration. The lack of prospective studies evaluating the effect of air pollution exposure in terms of live birth constitutes an important limitation in this review. Thus, further studies are needed to confirm these findings.

**Publication type:** Journal Article, Research Support, Non-U.S. Gov't

**Source:** MEDLINE

15. International committee for monitoring assisted reproductive technologies: World report on assisted reproductive technologies, 2007

**Citation:** Fertility and Sterility, February 2015, vol./is. 103/2(402-413.e11), 0015-0282;1556-5653 (01 Feb 2015)


**Language:** English
Abstract: Objective To analyze information on assisted reproductive technology (ART) performed worldwide, and trends in outcomes over successive years. Design Cross-sectional survey on access, efficiency, and safety of ART procedures performed in 55 countries during 2007. Setting Not applicable. Patient(s) Infertile women and men undergoing ART globally. Intervention(s) Collection and analysis of international ART data. Main Outcome Measure(s) Number of cycles performed, by country and region, including pregnancies, single and multiple birth rates, and perinatal mortality. Result(s) Overall, >1,251,881 procedures with ART were reported, and resulted in 229,442 reported babies born. The availability of ART varied by country, from 12 to 4,140 treatments per million population. Of all aspiration cycles, 65.2% (400,617 of 614,540) were intracytoplasmic sperm injection. The overall delivery rate per fresh aspiration was 20.3%, and for frozen-embryo transfer (FET), 18.4%, with a cumulative delivery rate of 25.8%. With wide regional variations, single-embryo transfer represented 23.4% of fresh transfers, and the proportion of deliveries with twins and triplets from fresh transfers was 22.3% and 1.2%, respectively. The perinatal mortality rate was 19.9 per 1,000 births for fresh in vitro fertilization using intracytoplasmic sperm injection, and 9.6 per 1,000 for FET. The proportion of women aged >40 years increased to 19.8% from 15.5% in 2006. Conclusion(s) The international trend toward <3 transferred embryos continued, as did the wider uptake of FET. This was achieved without compromising delivery rates. The application of ART for women aged >40 years was a major component of ART services in some regions and countries.

Publication type: Journal: Article

Source: EMBASE

16. Mental distress and personality in women undergoing GnRH agonist versus GnRH antagonist protocols for assisted reproductive technology

Citation: Human Reproduction, January 2015, vol./is. 30/1(103-110), 0268-1161;1460-2350 (01 Jan 2015)


Language: English

Abstract: STUDY QUESTION Do mental distress and mood fluctuations in women undergoing GnRH agonist and GnRH antagonist protocols for assisted reproductive technology (ART) differ depending on protocol and the personality trait, neuroticism? SUMMARY ANSWER ART treatment did not induce elevated levels of mental distress in either GnRH antagonist or agonist protocols but neuroticism was positively associated with increased mental distress, independent of protocols. WHAT IS KNOWN ALREADY ART treatment may increase mental distress by mechanisms linked to sex hormone fluctuations. General psychological characteristics, such as personality traits indexing negative emotionality, e.g. neuroticism, are likely to affect mental distress during ART treatment. STUDY DESIGN, SIZE, DURATION A total of 83 women undergoing their first ART cycle were consecutively randomized 1:1 to GnRH antagonist (n = 42) or GnRH agonist (n = 41) protocol. The study population was a subgroup of a larger ongoing Danish clinical randomized trial and was established as an add-on in the period 2010-2012. PARTICIPANTS/MATERIALS, SETTING, METHODS Women in the GnRH antagonist protocol received daily injections with recombinant follicle-stimulating hormone, Puregon<sup></sup> and subcutaneous injections with GnRH antagonist, Orgalutran<sup></sup> and subcutaneous injections with FSH, Puregon<sup></sup>. The study design did not allow for a blinding procedure. All women self-reported the Profile of Mood States, the Perceived Stress Scale, the Symptom Checklist-92-Revised, and the Major Depression Inventory questionnaires, at baseline, at ART cycle day 35, on the day of oocyte pick-up, and on the day of hCG testing. Also, a series of Profile of Mood States were reported daily during pharmacological treatment to monitor mood fluctuations. The personality trait Neuroticism was assessed at baseline by the self-reported NEO-PI-R questionnaire. MAIN RESULTS AND THE ROLE OF CHANCE ART did not induce within- or between-protocol changes in any of the applied measures of mental distress. However, the GnRH antagonist protocol was associated with more pronounced median mood fluctuations during the stimulation phase (agonist, 11.0 SD, [IQR = 21.1-6.1]; agonist, 8.9 SD, [IQR = 11.3-5.7], P = 0.025). This association became non-significant after applying a Bonferroni-Holm correction. Neuroticism was highly positively associated with increased levels of mental distress throughout treatment independent of protocols (all P-values <0.006), and cross-sectional analysis revealed that women with high or low Neuroticism scores at baseline showed a significant trend towards lower chances of a positive pregnancy test (P-value =0.028).

LIMITATIONS, REASONS FOR CAUTION Information on prognostic factors such as preceding length of infertility, number of retrieved oocytes and number of prior insemination treatments was not accounted for in the analyses. The stratification of protocols by age in the subgroups of women included in this study was suboptimal. Women with prior or current use of antidepressant medication were excluded from our study. WIDER IMPLICATIONS Our results imply that mental distress emerging during ART treatment is not causally linked to hypogonadism per se or to the choice of
protocol. Rather, our data highlight the potential importance of (i) rapid increases in ovarian steroids and (ii) addressing personality traits indexing negative emotionality, i.e. Neuroticism, in women undergoing ART treatment, to optimize both emotional adjustment and, possibly, the chances of obtaining pregnancy. STUDY FUNDING/COMPETING INTEREST(S) The Danish Research Council for Independent Research and MSD, Denmark kindly supported the study. The authors declare no competing financial interests. TRIAL REGISTRATION NUMBER EudraCT - 2008-005452-24.

Publication type: Journal: Article
Source: EMBASE

17. Meta-analysis of estradiol for luteal phase support in in vitro fertilization/intracytoplasmic sperm injection

Citation: Fertility and Sterility, February 2015, vol./is. 103/2(367-373.e5), 0015-0282;1556-5653 (01 Feb 2015)
Author(s): Huang N., Situ B., Chen X., Liu J., Yan P., Kang X., Kong S., Huang M.
Language: English
Abstract: Objective To evaluate whether the addition of E<sub>2</sub> for luteal phase support (LPS) in IVF/intracytoplasmic sperm injection (ICSI) could improve the outcome of clinical pregnancy. Design Meta-analysis. Setting University hospital center. Patient(s) Women underwent IVF or ICSI using the GnRH agonist or GnRH antagonist protocol. Intervention(s) Progesterone alone or combined with E<sub>2</sub> for LPS. Main Outcome Measure(s) Clinical pregnancy rate per patient (CPR/PA), clinical pregnancy rate per ET, implantation rate, ongoing pregnancy rate per patient, clinical abortion rate, and ectopic pregnancy rate. Result(s) Fifteen relevant randomized controlled trials (RCTs) were identified that included a total of 2,406 patients. There was no statistical difference between E<sub>2</sub> + P group and P-only group regarding the primary outcome of CPR/PA for different routes of administration of E<sub>2</sub> (oral, vaginal, and transdermal) or other relevant outcome measures. No significant effect was observed for different daily doses of E<sub>2</sub> (6, 4, and 2 mg), even through oral medication in CPR/PA. Conclusion(s) The best available evidence suggests that E<sub>2</sub> addition during the luteal phase does not improve IVF/ICSI outcomes through oral medication, even with different daily doses. Furthermore, RCTs that study other administration routes are needed.

Publication type: Journal: Article
Source: EMBASE

18. Omics as a window to view embryo viability

Citation: Fertility and Sterility, February 2015, vol./is. 103/2(333-341), 0015-0282;1556-5653 (01 Feb 2015)
Author(s): Krisher R.L., Schoolcraft W.B., Katz-Jaffe M.G.
Language: English
Abstract: The advent of advanced omics technologies and the application of these techniques to the analysis of extremely limited material have opened the door to the investigation of embryo physiology in a focused, in-depth approach never before possible. The application of noninvasive metabolomic and proteomic platforms to understanding embryo viability permits the characterization of individual embryos in culture. Initial clinical data have highlighted the promise of these technologies for the development of noninvasive embryo selection criteria. In this way, a complex view of embryo function can be compiled and related to embryo development, quality, and outcome. Application of knowledge gained from omics will transform both our understanding of embryo physiology as well as our ability to select viable embryos for transfer in assisted reproductive technology.

Publication type: Journal: Review
Source: EMBASE

19. Progesterone and the Luteal Phase: A Requisite to Reproduction

Citation: Obstetrics and Gynecology Clinics of North America, March 2015, vol./is. 42/1(135-151), 0889-8545;1558-0474 (01 Mar 2015)
Author(s): Mesen T.B., Young S.L.
Language: English
Abstract: Progesterone production from the corpus luteum is critical for natural reproduction. Progesterone supplementation seems to be an important aspect of any assisted reproductive technology treatment. Luteal phase deficiency in natural cycles is a plausible cause of infertility and pregnancy loss, though there is no adequate diagnostic test. This article describes the normal luteal phase of the menstrual cycle, investigates the controversy surrounding luteal phase deficiency, and presents the current literature for progesterone supplementation during assisted reproductive technologies.
20. Progesterone vaginal ring for luteal support.

**Citation:** Journal of Obstetrics & Gynaecology of India, February 2015, vol./is. 65/1(5-10), 0971-9202;0975-6434 (2015 Feb)

**Author(s):** Stadtmauer L, Waud K

**Language:** English

**Abstract:** Progesterone supplementation is universally used and has been shown to be beneficial in supplementation of the luteal phase in IVF. There are multiple options and the most commonly used include intramuscular and vaginal progesterone. A progesterone vaginal ring is a novel system for luteal support with advantages of controlled release with less frequent dosing. This review examines options for progesterone luteal support focusing on the rationale for a progesterone vaginal ring. Pub-med search of the literature. A weekly vaginal ring, although not yet FDA approved, is an effective and safe alternative for luteal supplementation in IVF. Large prospective clinical trials are needed to determine the best protocols for replacement cycles.

**Publication type:** Journal Article, Review

**Source:** MEDLINE

21. Quality analytics in ART: 1 Quantitating the relative impact of embryo quality on implantation rates (IR)

**Citation:** Fertility and Sterility, February 2015, vol./is. 103/2 SUPPL. 1(e40-e41), 0015-0282 (February 2015)

**Author(s):** Whistler J., Steinleitner A., Pan J.

**Language:** English

**Abstract:** BACKGROUND: Clinical assisted reproductive technologies (ART) practice could be considered as a "manufacturing process" wherein inputs of "materials" (patients, gametes, reagents, consumables) and labor are employed under specific environmental conditions to produce high quality embryos to initiate pregnancy. Industrial engineers have developed a statistical approach to assess quality within such manufacturing processes. Quality analytics and comparisons between ART centers require translating multiple descriptors (e.g. stage, fragmentation, etc.) into a one-dimensional metric for statistical evaluation. Although it obvious that morphological superior embryos produce higher implantation rate (IR), there are few large studies describing the relative impact of morphology on IR. OBJECTIVE: The purpose of this investigation is to create an empiric relative value scale for individual embryomorphology to serve as the basis the creation of a "mean embryo score" to describe embryo quality from an individual case. MATERIALS AND METHODS: Data was abstracted from the SART database records (2009 to 2011) drawn from a total of 40 clinics yielding a total of 18,379 patients and 45,617 embryos. Four consecutive clinics were selected from each "tenth-ile". IRs were calculated by segregating embryos according to the SART embryo descriptive measures in addition to patient age grouping, then dividing the number of implanted embryos by the number of transferred embryos for each permutation. RESULTS: A new embryo score is generated proportional to the implantation rate of this embryo type in practice. For young patients (<35), the highest among these is 0.41 from Hatching Blastocysts with good Inner Cell Mass and Trophectoderm Morphology. By comparison, a 6-cell embryo with moderate asymmetry and 0 fragmentation has a predicted IR of only 0.13. The complete tables will be presented. CONCLUSIONS: Data from this large cohort of embryos quantitates the probability that an embryo of a given stage and morphology will implant. This 1-dimensional metric of embryo quality is a tool for evaluating the relative value of an embryo, as well as the expected performance. This can be used to assess variation and quality within and between ART centers.

**Publication type:** Journal: Conference Abstract

**Source:** EMBASE

22. Reporting of embryo transfer methods in IVF research: a cross-sectional study.

**Citation:** Reproductive Biomedicine Online, February 2015, vol./is. 30/2(137-43), 1472-6483;1472-6491 (2015 Feb)

**Author(s):** Gambadauro P, Navaratnarajah R

**Language:** English

**Abstract:** The reporting of embryo transfer methods in IVF research was assessed through a cross-sectional analysis of randomized controlled trials (RCTs) published between 2010 and 2011. A systematic search identified 325 abstracts; 122 RCTs were included in the study. Embryo transfer methods were described in 42 out of 122 articles (34%). Catheters (32/42 [76%]) or ultrasound guidance (31/42 [74%]) were most frequently mentioned. Performer 'blinding' (12%) or technique standardization (7%) were seldom reported. The description of embryo transfer methods was...
significant more common in trials published by journals with lower impact factor (less than 3, 39.6%; 3 or greater, 21.5%; P = 0.037). Embryo transfer methods were reported more often in trials with ovarian stimulation as the main end-point (33% versus 16%) or with positive outcomes (37.8% versus 25.0%), albeit not significantly. Multivariate logistic regression confirmed that RCTs published in higher impact factor journals are less likely to describe embryo transfer methods (OR 0.371; 95% CI 0.143 to 0.964). Registered trials, trials conducted in an academic setting, multi-centric studies or full-length articles were not positively associated with embryo transfer methods reporting rate. Recent reports of randomized IVF trials rarely describe embryo transfer methods. The under-reporting of research methods might compromise reproducibility and suitability for meta-analysis. Copyright © 2014 Reproductive Healthcare Ltd. Published by Elsevier Ltd. All rights reserved.

**Publication type:** Journal Article  
**Source:** MEDLINE

### 23. Risk of preeclampsia in pregnancies after assisted reproductive technology and ovarian stimulation

**Citation:** American Journal of Obstetrics and Gynecology, January 2015, vol./is. 212/1 SUPPL. 1(S371-S372), 0002-9378 (January 2015)  
**Author(s):** Martin A., Monsour M., Boulet S., Kawwass J., Kissin D., Jamieson D.  
**Language:** English  
**Abstract:** OBJECTIVE: Conflicting evidence exists surrounding the risk of preeclampsia after assisted reproductive technology (ART). It has been hypothesized that elevated circulating estrogen levels after ovarian stimulation (OS) associated with ART contribute to abnormal placentation, increasing the risk of preeclampsia. We compared the risk of preeclampsia among spontaneous conception deliveries with that among deliveries after OS with ART, OS without ART, OS with only aromatase inhibitors which do not cause supraphysiologic estrogen levels, and unstimulated intrauterine insemination (IUI). STUDY DESIGN: Live-born singleton deliveries among women 20-49 years were identified in the 2005-2011 Truven Health Market Scan Commercial Claims and Encounters Databases using ICD-9 and CPT codes. Maternal characteristics were compared using chi-squared and Fisher exact tests. We performed multilevel multivariable logistic regression, controlling for maternal age, parity, comorbid conditions, and region of delivery, and calculated adjusted odds ratios (aOR) and 95% confidence intervals (CI) for mild and severe preeclampsia. RESULTS: The adjusted odds of developing preeclampsia were increased for deliveries after OS with ART (mild preeclampsia aOR 1.32, CI 1.14-1.52; severe preeclampsia aOR 1.89, CI 1.63-2.18) and OS without ART (mild preeclampsia aOR 1.29, CI 1.20-1.39; severe preeclampsia 1.48, CI 1.36-1.61). There was also an increase in preeclampsia after unstimulated IUI (mild preeclampsia aOR 1.30, CI 1.05-1.62; severe aOR 1.40, CI 1.08-1.81). 30% of all IUI deliveries in our database were unstimulated. Odds of preeclampsia were similar between spontaneous conception and aromatase inhibitor deliveries. CONCLUSION: The risk of preeclampsia after ART may be related to supraphysiologic estrogen levels associated with non-aromatase inhibitor OS rather than the ART treatment itself. The increased risk of preeclampsia after unstimulated IUI may reflect under-reporting of OS in our database. (Table Presented).  
**Publication type:** Journal: Conference Abstract  
**Source:** EMBASE

### 24. Salpingectomy and Proximal Tubal Occlusion for Hydrosalpinx Prior to In Vitro Fertilization: A Meta-analysis of Randomized Controlled Trials.

**Citation:** Obstetrical & Gynecological Survey, January 2015, vol./is. 70/1(33-8), 0029-7828;1533-9866 (2015 Jan)  
**Author(s):** Zhang Y, Sun Y, Guo Y, Li TC, Duan H  
**Language:** English  
**Abstract:** OBJECTIVE: The objective of this study was to conduct a systematic review of studies comparing the pregnancy outcomes in hydrosalpinx patients treated with salpingectomy versus those treated with proximal tubal occlusion prior to in vitro fertilization (IVF).DATA SOURCES: An extensive PubMed literature search was performed for the period from 1980 to December 2013 using combinations of the following keywords: "hydrosalpinx," "salpingectomy," and "tubal occlusion."METHODS OF THE STUDY SELECTION: Initially, 204 relevant studies were identified from MEDLINE and screened for retrieval. All of the randomized controlled trials comparing ovarian response and the pregnancy outcome of salpingectomy and proximal tubal occlusion for hydrosalpinx patients prior to IVF were considered eligible for analysis.TABULATION, INTEGRATION, AND RESULTS: Two investigators independently reviewed the studies. The data were pooled, and the mean standard difference (SD) was calculated. Eligible randomized controlled trials were selected for this meta-analysis. There were no differences in the response days to controlled ovarian hyperstimulation (SD = -1.112, SE = 0.797, Z = -1.14, P = 0.253), number of oocytes retrieved (SD = 0.304, SE = 0.311, Z = 1.300, P = 0.194), embryos transferred per cycle (SD = -0.757, SE = 0.568, Z = -1.332, P = 0.183), and fertilized
oocytes (SD = -0.006, SE = 0.130, Z = -0.045, P = 0.964) between the patients receiving salpingectomy and proximal tubal occlusion. The pooled rates for clinical pregnancy (odds ratio, 0.864; 95% confidence interval, 0.534-1.398; Z = -0.596, P = 0.551) and implantation (odds ratio, 1.558; 95% confidence interval, 0.809-3.003; Z = 1.325, P = 0.185) were not significantly different between the hydrosalpinx patients with salpingectomy versus proximal tubal occlusion.

CONCLUSIONS: Similar responses to controlled ovarian hyperstimulation and pregnancy outcome were observed in patients treated with salpingectomy or proximal tubal occlusion.

Publication type: Journal Article
Source: MEDLINE
Full text: Available Obstetrical & gynecological survey at Obstetrical and Gynecological Survey

25. Scientific Papers to be Presented at the 63rd Annual Meeting of the Pacific Coast Reproductive Society

Citation: Fertility and Sterility, February 2015, vol./is. 103/2 SUPPL. 1, 0015-0282 (February 2015)
Language: English
Abstract: The proceedings contain 80 papers. The topics discussed include: embryonic aneuploidy does not differ amongst major ethnicities as determined by genotyping; one pronucleus zygotes, derived both from ivi and insemination, rarely develop to quality blastocysts and they are significantly less likely to be frozen or transferred; does a reduced HCG trigger dose compromise outcomes in a large prospective trial of vaginal progesterone for luteal phase support?; donor attributes impacting success in a frozen oocyte donation program; predictive value of anti-Mullerian hormone Levels (AMH) in a young non infertile donor population; follicular growth and endocrine IVF cycle characteristics during ovarian stimulation in older women; effect of salpingectomy on ovarian reserve: a systematic review and meta-analysis; and developmentally delayed cleavage-stage embryos maintain high implantation rates in frozen embryo transfers.
Publication type: Journal: Conference Review
Source: EMBASE

26. Should IVF be used as first-line treatment or as a last resort? A debate presented at the 2013 Canadian Fertility and Andrology Society meeting

Citation: Reproductive BioMedicine Online, February 2015, vol./is. 30/2(128-136), 1472-6483;1472-6491 (01 Feb 2015)
Author(s): Huang L.N., Tan J., Hitkari J., Dahan M.H.
Language: English
Abstract: Infertility outcomes can be influenced by many factors. Although a number of treatments are offered, deciding which one to use first is a controversial topic. Although IVF may have superior efficacy in achieving a live birth with a reasonable safety profile, the availability of cheaper and less invasive treatments preclude its absolute use. For this reason, certain patient groups with 'good-prognosis' infertility are traditionally treated with less invasive treatments first. 'Good-prognosis' infertility may include unexplained infertility, mild male factor infertility, stage I or II endometriosis, unilateral tubal blockage and diminished ovarian reserve. Here, evidence behind the use of IVF as a first-line treatment is compared with its use as a last-resort option in women with 'good-prognosis' infertility.
Publication type: Journal: Review
Source: EMBASE

27. Sperm DNA fragmentation index and pregnancy outcome after IVF or ICSI: a meta-analysis.

Citation: Journal of Assisted Reproduction & Genetics, January 2015, vol./is. 32/1(17-26), 1058-0468;1573-7330 (2015 Jan)
Author(s): Zhang Z, Zhu L, Jiang H, Chen H, Chen Y, Dai Y
Language: English
Abstract: PURPOSE: The purpose of this study was to carry out a meta-analysis for a comprehensive understanding and estimation of the association between sperm DNA Fragmentation Index (DFI) and pregnancy outcome after in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment.METHODS: Studies concerning the link of DFI with pregnancy outcome were included after literature search of database PUBMED, EMBASE, MEDLINE. Related information was extracted from the eligible studies by two independent authors and a meta-analysis was conducted by using STATA 12.0 software. Pregnancy outcomes consisted of biochemical pregnancy (BP), clinical pregnancy (CP) and pregnancy loss (PL). The studies included for meta-analysis were divided into three groups according to the DFI threshold value (DFI >27 %, 15-27 %, <15 % group). The odds ratio (OR ) and their 95 % confidence intervals (95 % CIs) were used to evaluate the association between DFI and pregnancy outcome.RESULTS: Twenty articles were included in our meta-analysis. The results indicated that infertile couples were more likely to get pregnant if DFI was less than
thirty-sixty (2015 Feb) 1460;2350 (2015 Feb) 1460;2350.528 (0.264-1.097) respectively) outcome yielded nonsignificant results. CONCLUSIONS: The predication value of DFI for IVF or ICSI outcome is not confirmed in our meta-analysis. Further better designed studies with larger subjects involved are needed to better address this issue.

Publication type: Journal Article, Research Support, Non-U.S. Gov't
Source: MEDLINE

28. Surgical management of tubal disease and infertility
Citation: Obstetrics, Gynaecology and Reproductive Medicine, January 2015, vol./is. 25/1(6-11), 1751-7214;1879-3622 (01 Jan 2015)
Author(s): Kong G.W.S., Li T.C.
Language: English
Abstract: With the advance in assisted reproductive technology (ART), the role of reproductive surgery as the primary treatment of infertility has been questioned. Tubo-peritoneal factor is common, and accounts for 30-40% of female infertility. The pathology of tubal disease ranges from peritubal adhesion, proximal and/or distal tubal blockage, hydrosalpinx to previous sterilization. In tubo-peritoneal infertility, reproductive surgery remains an important option and is complementary to ART. It should be considered as the first-line treatment if a good result is expected when the pathology is amendable or if untreated will adversely affect the results or increase the risks of ART. The success of reproductive surgery depends on careful patient selection using proper investigative tools, performed in units with expertise following microsurgical principles.

Publication type: Journal Article, Research Support, Non-U.S. Gov't
Source: MEDLINE

Citation: Human Reproduction, February 2015, vol./is. 30/2(473-83), 0268-1161;1460-2350 (2015 Feb)
Author(s): Lee E, Illingworth P, Wilton L, Chambers GM
Language: English
Abstract: STUDY QUESTION: Is preimplantation genetic diagnosis for aneuploidy (PGD-A) with analysis of all chromosomes during assisted reproductive technology (ART) clinically and cost effective? SUMMARY ANSWER: The majority of published studies comparing a strategy of PGD-A with morphologically assessed embryos have reported a higher implantation rate per embryo using PGD-A, but insufficient data has been presented to evaluate the clinical and cost-effectiveness of PGD-A in the clinical setting. WHAT IS KNOWN ALREADY: Aneuploidy is a leading cause of implantation failure, miscarriage and congenital abnormalities in humans, and a significant cause of ART failure. Preclinical evidence of PGD-A indicates that the selection and transfer of euploid embryos during ART should improve clinical outcomes. STUDY DESIGN, SIZE AND DURATION: A systematic review of the literature was performed for full text English language articles using MEDLINE, EMBASE, SCOPUS, Cochrane Library databases, NHS Economic Evaluation Database and EconLit. The Downs and Black scoring checklist was used to assess the quality of studies. Clinical effectiveness was measured in terms of pregnancy, live birth and miscarriage rates. PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Nineteen articles meeting the inclusion criteria, comprising three RCTs in young and good prognosis patients and 16 observation studies were identified. Five of the observational studies included a control group of patients where embryos were selected based on morphological criteria (matched cohort studies). MAIN RESULTS AND ROLE OF CHANCE: Of the five studies that included a control group and reported implantation rates, four studies (including two RCTs) demonstrated improved implantation rates in the PGD-A group. Of the eight studies that included a control group, six studies (including two RCTs) reported significantly higher pregnancy rates in the PGD-A group, and in the remaining two studies, equivalent pregnancies rates were reported despite fewer embryos being transferred in the PGD-A group. The three RCTs demonstrated benefit in young and good prognosis patients in terms of clinical pregnancy rates and the use of single embryo transfer. However, studies relating to patients of advanced maternal age, recurrent miscarriage and implantation failure were restricted to matched cohort studies, limiting the ability to draw meaningful conclusions. LIMITATIONS, REASONS FOR CAUTION: Relevant studies may have been missed
and findings from RCTs currently being undertaken could not be included.

**WIDER IMPLICATIONS OF THE FINDINGS:** Given the uncertain role of PGD-A techniques, high-quality experimental studies using intention-to-treat analysis and cumulative live birth rates including the comparative outcomes from remaining cryopreserved embryos are needed to evaluate the overall role of PGD-A in the clinical setting. It is only in this way that the true contribution of PGD-A to ART can be understood.

**STUDY FUNDING/COMPETING INTERESTS:** No specific funding was used to undertake this study.

Evelyn Lee does not report any conflict of interest. Associate Professor Illingworth is an employee of and a shareholder in Virtus Health which is a provider of clinical preimplantation genetic services to patients in Australia Dr Lee and Dr Chambers previously received grant support to her institution from the Australian Government, Australian Research Council (ARC) Linkage Grant No. LP1002165; ARC Linkage Grant Partner Organisations were IVF Australia, Melbourne IVF and Queensland Fertility Group. **TRIAL REGISTRATIONS NUMBER:** NA. Copyright © The Author 2014. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

**Publication type:** Journal Article, Research Support, Non-U.S. Gov't

**Source:** MEDLINE

### 30. The effect of sperm DNA fragmentation on live birth rate after IVF or ICSI: A systematic review and meta-analysis

**Citation:** Reproductive BioMedicine Online, February 2015, vol./is. 30/2(120-127), 1472-6483;1472-6491 (01 Feb 2015)

**Author(s):** Osman A., Alsomait H., Seshadri S., El-Toukhyy T., Khalaf Y.

**Language:** English

**Abstract:** A systematic review and meta-analysis was conducted to evaluate the relationship between the extent of sperm DNA damage and live birth rate (LBR) per couple and the influence of the method of fertilization on treatment outcome. Searches were conducted on MEDLINE, EMBASE and Cochrane Library. Six studies were eligible for inclusion in the meta-analysis. Overall, LBR increased significantly in couples with low sperm DNA fragmentation compared with those with high sperm DNA fragmentation (RR 1.17, 95% CI 1.07 to 1.28; P = 0.0005). After IVF and intracytoplasmic sperm injection (ICSI), men with low sperm DNA fragmentation had significantly higher LBR (RR 1.27, 95% CI 1.05 to 1.52; P = 0.01) and (RR 1.11, 95% CI 1.00 to 1.23, P = 0.04), respectively. A sensitivity analysis showed no statistically significant difference in LBR between low and high sperm DNA fragmentation when ICSI treatment was used (RR 1.08, 95% CI 0.39 to 2.96; P = 0.88). High sperm DNA fragmentation in couples undergoing assisted reproduction techniques is associated with lower LBR. Well-designed randomized studies are required to assess the role of ICSI over IVF in the treatment of men with high sperm DNA fragmentation.

**Publication type:** Journal: Review

**Source:** EMBASE

### 31. The role of acupuncture in in vitro fertilization: a systematic review and meta-analysis.

**Citation:** Gynecologic & Obstetric Investigation, 2015, vol./is. 79/1(1-12), 0378-7346;1423-002X (2015)

**Author(s):** Shen C, Wu M, Shu D, Zhao X, Gao Y

**Language:** English

**Abstract:** BACKGROUND/AIMS: In recent years, acupuncture has become more and more popular in the management of subfertility. The aim of this study was to evaluate the impact of acupuncture during in vitro fertilization (IVF) treatment on the outcomes of clinical pregnancy in published randomized studies. METHODS: This is a systematic review and meta-analysis. Data sources used were MEDLINE, Embase, Web of Knowledge and the Chinese Biomedical Database. RESULTS: There was no statistically significant difference between the acupuncture group and no acupuncture (intervention) controls around the time of embryo transfer (ET; risk ratio, RR, 1.24, 95% confidence interval, CI, 1.02-1.50) or in unblinded trials, trials blinded to physicians and double-blind trials (95% CI 1.26-1.88, 0.82-1.33 and 0.89-1.25, respectively). This was also the case when comparing acupuncture with sham acupuncture controls around the time of ET (RR, 1.03, 95% CI 0.87-1.22) or when restricting to unblinded trials, trials blinded to physicians and double-blind trials (95% CI 0.80-2.02, 0.82-1.18 and 0.77-1.17, respectively). There was a statistically significant difference when performed at 30 min after ET and implantation phase (RR 1.76, 95% CI 1.22-2.55). There was also a statistically significant difference when performed at follicle phase and 25 min before and after ET (RR 1.56, 95% CI 1.04-2.33). CONCLUSION: Our study showed that acupuncture did not significantly improve the IVF clinical pregnancy rate when performed only at the time of ET, while we found pooled benefit of acupuncture for IVF when performed at follicle phase and 25 min before and after ET, as well as 30 min after ET and implantation phase. Copyright © The Author 2014. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

**Publication type:** Journal Article, Research Support, Non-U.S. Gov't

**Source:** MEDLINE
32. Time-lapse systems for embryo incubation and assessment in assisted reproduction.

Citation: Cochrane Database of Systematic Reviews, 2015, vol./is. 2/(CD011320), 1361-6137;1469-493X (2015)

Author(s): Armstrong S, Arroll N, Cree LM, Jordan V, Farquhar C

Language: English

Abstract: BACKGROUND: Embryo incubation and assessment is a vital step in assisted reproductive technology (ART). Traditionally, embryo assessment has been achieved by removing embryos from a conventional incubator daily for assessment of quality by an embryologist, under a light microscope. Over recent years time-lapse systems (TLSs) have been developed which can take digital images of embryos at frequent time intervals. This allows embryologists, with or without the assistance of computer algorithms, to assess the quality of the embryos without physically removing them from the incubator. The potential advantages of a TLS include the ability to maintain a stable culture environment, therefore limiting the exposure of embryos to changes in gas composition, temperature and movement. Additionally a TLS has the potential advantage of improving embryo selection for ART treatment by utilising additional information gained through monitoring embryo development.

OBJECTIVES: To determine the effect of a TLS compared to conventional embryo incubation and assessment on clinical outcomes in couples undergoing ART.

SEARCH METHODS: A comprehensive search of all the major electronic databases, including grey literature, was undertaken in co-ordination with the Trials Search Co-ordinator of the Cochrane Menstrual Disorders and Subfertility Group in July 2014 and repeated in November 2014 to confirm that the review is up to date.

SELECTION CRITERIA: Two authors (SA and NA) independently scanned the titles and abstracts of the articles retrieved by the search. Full texts of potentially eligible randomised controlled trials (RCTs) were obtained and examined independently by the authors for their suitability according to the review inclusion criteria. In the case of doubt between the two authors, a third author (LC) was consulted to gain consensus. The selection process is documented with a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart.

DATA COLLECTION AND ANALYSIS: Data were obtained and extracted by two authors. Disagreement was resolved by consensus. Trial authors were contacted by e-mail to obtain further study information and data. All extracted data were dichotomous outcomes and odds ratios (OR) were calculated according to the review inclusion criteria. In the case of doubt between the two authors, a third author (LC) was consulted to gain consensus. The selection process is documented with a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart.

MAIN RESULTS: Three studies involving 994 women were found for inclusion. Data from all three studies were used to address comparison one, TLS with or without cell-tracking algorithms versus conventional incubation. No studies were found to address comparison two, TLS utilising cell-tracking algorithms versus TLS not utilising cell-tracking algorithms. There was only one study which reported live birth (n = 76). The results demonstrated no conclusive evidence of a difference in live birth rate per couple randomly assigned to the TLS and conventional incubation arms of the study (OR 1.1, 95% CI 0.45 to 2.73, 1 RCT, n = 76, moderate quality evidence). All three studies reported miscarriage (n = 994). There was no conclusive evidence of a difference in miscarriage rates per couple randomly assigned to the TLS and conventional incubation arms (OR 0.70, 95% CI 0.47 to 1.04, 3 RCTs, n = 994, I(2) = 0%, low quality evidence). Only one study reported stillbirth rates (n = 76). There were equal numbers of stillbirths in both the TLS and conventional incubation arms of the study. Therefore, there was no evidence of a difference in the stillbirth rate per couple randomly assigned to TLS and conventional incubation (OR 1.0, 95% CI 0.13 to 7.49, 1 RCT, moderate quality evidence). All three studies reported clinical pregnancy rates (n = 994). There was no conclusive evidence of a difference in clinical pregnancy rate per couple randomly assigned to the TLS and conventional incubation arms (OR 1.23, 95% CI 0.96 to 1.59, 3 RCTs, n = 994, I(2) = 0%, low quality evidence). None of the included studies reported cumulative clinical pregnancy rates.

AUTHORS' CONCLUSIONS: There is insufficient evidence of differences in live birth, miscarriage, stillbirth or clinical pregnancy to choose between TLS and conventional incubation. Further data explicitly comparing the incubation environment, the algorithm for embryo selection, or both, are required before recommendations for a change of routine practice can be justified.

33. Ultrasound guidance during embryo transfer: a systematic review and meta-analysis of randomized controlled trials.

Citation: Ultrasound in Obstetrics & Gynecology, February 2015, vol./is. 45/2(139-48), 0960-7692;1469-0705 (2015 Feb)

Author(s): Teixeira DM, Dassuncao LA, Vieira CV, Barbosa MA, Coelho Neto MA, Nastri CO, Martins WP
OBJECTIVES: To summarize the current evidence on the effect of using ultrasound (US) guidance during embryo transfer (ET).

METHODS: In this systematic review, we included randomized controlled trials examining the effect of the use of US guidance during ET; data from studies using the same catheter type in study arms were not pooled with the results from studies that used different catheter types.

RESULTS: Twenty-one studies were included in the quantitative analysis: 18 compared 'US guidance' with 'clinical touch', of which one was subsequently excluded from the quantitative meta-analysis owing to a lack of available data, three studies compared transvaginal US guidance with transabdominal US guidance, and one study compared 'hysterosonometry before ET' with US guidance.

Comparison of the use of US guidance with clinical touch, in studies that used the same catheter type in the study arms, indicated a benefit of using US guidance during ET on the rates of live birth (relative risk (RR), 1.48 (95% CI, 1.16-1.87)), based on two studies involving 888 women with moderate-quality evidence, and on the rates of clinical pregnancy (RR, 1.32 (95% CI, 1.18-1.46)), based on 13 studies involving 3641 women with high-quality evidence. However, when comparing the use of US guidance with clinical touch in studies that used different catheter types, the results suggest that using US guidance during ET has no effect on the rates of reproductive outcome: live birth (RR, 0.99 (95% CI, 0.83-1.19)), based on one study involving 1649 women with moderate-quality evidence; clinical pregnancy (RR, 1.04 (95% CI, 0.89-1.21)), based on five studies involving 2949 women with moderate-quality evidence. The estimates for the rate of miscarriage and for the other identified comparisons were imprecise.

CONCLUSIONS: The available evidence suggests that there is a benefit of using US guidance during ET. However, both US-guided transfer and clinical touch should be considered acceptable, as the benefit of US is not large and should be balanced against the increased cost and need to change the catheter type. More studies are required before conclusions can be drawn regarding the effect of other techniques on reproductive outcome. Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.

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News

BBC Health

**Male fertility: Losing weight and cancer drugs 'boost sperm'**

Saturday 7th March 2015

Two approaches to boosting obese men's sperm have been presented at the annual meeting of the Endocrine Society. The first suggested that obese men who lost weight were more likely get their partners pregnant. The second found that a cancer drug helped some infertile men have children.

NHS Choices

**Could 'DNA editing' lead to designer babies?**

Monday 19th January 2015

"Rapid progress in genetics is making 'designer babies' more likely and society needs to be prepared," BBC News reports. The headline is prompted by advances in "DNA editing", which may eventually lead to genetically modified babies (though that is a very big “may”).

**MPs vote to give the go-ahead to three-parent IVF**

Wednesday 4th February 2015

"In an historic move, MPs have voted in favour of the creation of babies with DNA from two women and one man,” BBC News reports. The UK is set to become the first country to license the technique known as three-parent IVF, which could potentially be used to prevent babies being born with mitochondrial diseases.

**Nordic IVF outcomes improving - is the same true for the UK?**

Wednesday 21st January 2015

"The health of artificially conceived children has steadily improved in the last 20 years," The Guardian reports. Researchers who analysed data from Nordic countries described the decline in premature and stillbirths as "remarkable". This was the main finding of a large cohort study comparing the health of babies born using assisted reproduction technology (ART), such as in vitro fertilisation (IVF), with those conceived naturally over the last 20 years.
Obesity damage to eggs may be reversible
Wednesday 11th February 2015
“Damaging effect of obesity on a woman’s eggs can now be reversed,” is the potentially misleading headline from the Mail Online today. The over-egged headline refers to a mouse study showing that signs of lower fertility due to obesity could be reversed using experimental drugs. This was not tested in humans, however.

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