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Current Awareness Bulletin – Fertility
December 2014 & January 2015

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Cochrane Systematic Reviews

New Review – December 2014
Ovarian cyst aspiration prior to in vitro fertilization treatment for subfertility

Updated Review – December 2014
Antioxidants for male subfertility

Assisted reproductive technology: an overview of Cochrane Reviews

Synchronised approach for intrauterine insemination in subfertile couples

Updated Review – November 2014
Metformin treatment before and during IVF or ICSI in women with polycystic ovary syndrome

UpToDate

What’s New in Reproductive Endocrinology

Fertility related topics

Journals – latest issue with full text access

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

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**Journal Articles:**

1. Antimullerian hormone as predictor of implantation and clinical pregnancy after assisted conception: a systematic review and meta-analysis.

   **Citation:** Fertility & Sterility, January 2015, vol./is. 103/1(119-130.e3), 0015-0282;1556-5653 (2015 Jan)

   **Author(s):** Tal R, Tal O, Seifer BJ, Seifer DB

   **Language:** English

   **Abstract:** OBJECTIVE: To assess whether antimullerian hormone (AMH) is a predictor of implantation and/or clinical pregnancy in women undergoing assisted reproductive technology. DESIGN: Systematic review and meta-analysis. SETTING: Not applicable. PATIENT(S): Women undergoing IVF/intracytoplasmic sperm injection in non-donor cycles. INTERVENTION(S): Measurement of serum AMH level. MAIN OUTCOME MEASURE(S): Diagnostic odds ratio (OR) and summary receiver operating characteristic curve (AUC) for AMH as a predictor of implantation and/or clinical pregnancy. RESULT(S): A total of 525 observational studies were identified, of which 19 were selected (comprising 5,373 women). Studies reporting clinical pregnancy rates in women with unspecified ovarian reserve (n = 11), diminished ovarian reserve (DOR) (n = 4), and polycystic ovary syndrome (n = 4) were included, together with studies reporting implantation rates (n = 4). The OR for AMH as a predictor of implantation in women with unspecified ovarian reserve (n = 1,591) was 1.83 (95% confidence interval [CI] 1.49-2.25), whereas the AUC was 0.591 (95% CI 0.563-0.618). The OR for AMH as a predictor of clinical pregnancy in these women (n = 4,324) was 2.10 (95% CI 1.82-2.41), whereas the AUC was 0.634 (95% CI 0.618-0.650). The predictive ability of AMH for pregnancy was greatest in women with DOR (n = 615), with OR and AUC of 3.96 (95% CI 2.57-6.10) and 0.696 (95% CI 0.641-0.751), respectively. In contrast, AMH had no significant predictive ability in women with PCOS (n = 414), with OR and AUC of 1.18 (95% CI 0.53-2.62) and 0.600 (95% CI 0.547-0.653), respectively. CONCLUSION(S): Antimullerian hormone has weak association with implantation and clinical
pregnancy rates in assisted reproductive technology but may still have some clinical utility in counseling women undergoing fertility treatment regarding pregnancy rates, particularly those with DOR. Copyright 2015 American Society for Reproductive Medicine. Published by Elsevier Inc. All rights reserved.

**Publication type:** Journal Article

**Source:** MEDLINE

**Full text:** Available FERTILITY AND STERILITY at Salisbury District Hospital Healthcare Library


**Citation:** Cochrane Database of Systematic Reviews, 2014, vol./is. 12/(CD010537), 1361-6137;1469-493X (2014)

**Author(s):** Farquhar C, Rishworth JR, Brown J, Nelen WL, Marjoribanks J

**Language:** English

**Abstract:** BACKGROUND: As many as one in six couples will encounter problems with fertility, defined as failure to achieve a clinical pregnancy after regular intercourse for 12 months. Increasingly, couples are turning to assisted reproductive technology (ART) for help with conceiving and ultimately giving birth to a healthy live baby of their own. Fertility treatments are complex, and each ART cycle consists of several steps. If one of the steps is incorrectly applied, the stakes are high as conception may not occur. With this in mind, it is important that each step of the ART cycle is supported by good evidence from well-designed studies. OBJECTIVES: To summarise the evidence from Cochrane systematic reviews on procedures and treatment options available to couples with subfertility undergoing assisted reproductive technology (ART). METHODS: Published Cochrane systematic reviews of couples undergoing ART (in vitro fertilisation or intracytoplasmic sperm injection) were eligible for inclusion in the overview. We also identified Cochrane reviews in preparation, for future inclusion. The outcomes of the overview were live birth (primary outcome), clinical pregnancy, multiple pregnancy, miscarriage and ovarian hyperstimulation syndrome (secondary outcomes). Studies of intrauterine insemination and ovulation induction were excluded. Selection of systematic reviews, data extraction and quality assessment were undertaken in duplicate. Review quality was assessed by using the AMSTAR tool. Reviews were organised by their relevance to specific stages in the ART cycle. Their findings were summarised in the text and data for each outcome were reported in 'Additional tables'. MAIN RESULTS: Fifty-eight systematic reviews published in The Cochrane Library were included. All were high quality. Thirty-two reviews identified interventions that were effective (n = 19) or promising (n = 13), 14 reviews identified interventions that were either ineffective (n = 3) or possibly ineffective (n = 11), and 12 reviews were unable to draw conclusions due to lack of evidence. An additional 11 protocols and one title were identified for future inclusion in this overview. AUTHORS' CONCLUSIONS: This overview provides the most up to date evidence on ART cycles from systematic reviews of randomised controlled trials. Fertility treatments are costly and the stakes are high. Using the best available evidence to optimise outcomes is best practice. The evidence from this overview could be used to develop clinical practice guidelines and protocols for use in daily clinical practice, in order to improve live birth rates and reduce rates of multiple pregnancy, cycle cancellation and ovarian hyperstimulation syndrome.

**Publication type:** Journal Article

**Source:** MEDLINE

**Full text:** Available Wiley at Cochrane Library, The

### 3. Cardiovascular dysfunction in offspring of ovarian-hyperstimulated women and effects of estradiol and progesterone: A retrospective cohort study and proteomics analysis

**Citation:** Journal of Clinical Endocrinology and Metabolism, December 2014, vol./is. 99/12(E2494-E2503), 0021-972X;1945-7197 (01 Dec 2014)


**Language:** English

**Abstract:** Context: The cardiovascular dysfunction in children born with assisted reproductive technologies has been of great concern. However, the association of ovarian hyperstimulation syndrome (OHSS), a complication of assisted reproductive technologies, with worse cardiovascular functions and underlying mechanism remains unknown. Objectives: The objective of the study was to assess the cardiovascular functions of children born to mothers with OHSS and investigate the underlying regulator(s). Design and Setting: This was a retrospective cohort recruited in a university hospital. Participants and Methods: We assessed the cardiovascular functions by Doppler echography in 42 children born to OHSS women, 34 children of mothers with non-OHSS in vitro fertilization, and 48 spontaneously conceived (SC) children (mean age ~4.5 y). Groups were matched for
gestational age at delivery and birth weight. An isobaric tag for relative and absolute quantitation-labeled proteomics analysis was performed with another set of umbilical arteries from OHSS and SC pregnancies (n = 3 for both groups). Results: Children of OHSS mothers showed a significantly decreased mitral ratio of early to late mitral peak velocities, reduced systolic and diastolic diameters of common carotid arteries, and impaired flow-mediated dilation compared with non-OHSS in vitro fertilization and SC children. Intima-media thickness and arterial stiffness indices were similar in the three groups. In the proteomics study, 1640 proteins were identified from OHSS and SC umbilical arteries, and 40 differentially expressed proteins were selected for further analysis. Estradiol and progesterone were identified as activated upstream regulators. Conclusions: Children born to ovarian-hyperstimulated women displayed cardiovascular dysfunctions. The underlying mechanisms may involve the effects of supraphysiological estradiol and progesterone levels.

**Publication type:** Journal: Article

**Source:** EMBASE

**Full text:** Available *The Journal of clinical endocrinology and metabolism* at No link? Ask Salisbury Healthcare Library - please click here to request article.

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4. **Casting for determinants of blastocyst yield and of rates of implantation and of pregnancy after blastocyst transfers**

**Citation:** Fertility and Sterility, October 2014, vol./is. 102/4(1055-1064), 0015-0282;1556-5653 (01 Oct 2014)

**Author(s):** Stone B.A., March C.M., Ringler G.E., Baek K.J., Marrs R.P.

**Language:** English

**Abstract:** Objective: To identify determinants of blastocyst yield, implantation rate, and pregnancy outcome. Design: Retrospective analysis of outcomes of 1,653 cycles of IVF. Setting: Private infertility clinic. Patient(s): Couples presenting to an infertility clinic for IVF. Intervention(s): None. Main Outcome Measure(s): Blastocyst yield, implantation rate, and pregnancy. Result(s): Of a broad array of potential determinants, only the total numbers of oocytes retrieved and properties of day 3 embryos were consistently predictive of blastocyst formation. Relative to numbers of oocytes fertilized by intracytoplasmic sperm injection (ICSI), yields of quality blastocysts were highest in cycles in which <10 oocytes were retrieved. Blastocyst yield was closely linearly correlated with average numbers of blastomeres in embryos on day 3. As oocyte yields rose, average grades and the implantation potential of the blastocysts selected for transfer increased by approximately 0.015 and 0.15%, respectively, for each additional oocyte. Independently, the implantation potential of blastocysts decreased 1.1% for each advancing year in age of the oocyte provider, and, for autologous transfers, uterine receptivity declined an additional 0.6% per year. Higher yields of blastocysts from cycles with high oocyte numbers afforded better selection of blastocysts for transfer, supporting higher overall implantation and pregnancy rates. Conclusion(s): While the proportion of fertilized oocytes that progressed to quality blastocysts diminished as numbers of recovered oocytes rose, rates of implantation and pregnancy after transfer of the selected best blastocysts increased. The age of the oocyte provider and oocyte yields independently impacted blastocyst implantation potential and uterine receptivity after controlled ovarian hyperstimulation, ICSI, and blastocyst transfer.

**Publication type:** Journal: Article

**Source:** EMBASE

**Full text:** Available *FERTILITY AND STERILITY* at Salisbury District Hospital Healthcare Library

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5. **Cell adhesion molecules and in vitro fertilization**

**Citation:** In Vivo, September 2014, vol./is. 28/5(683-690), 0258-851X;1791-7549 (01 Sep 2014)

**Author(s):** Simopoulou M., Nikolopoulou E., Dimakakos A., Charalabopoulos K., Koutsilieris M.

**Language:** English

**Abstract:** This review addresses issues regarding the need in the in vitro fertilization (IVF) field for further predictive markers enhancing the standing embryo selection criteria. It aims to serve as a source of defining information for an audience interested in factors related to the wide range of multiple roles played by cell adhesion molecules (CAMs) in several aspects of IVF ultimately associated with the success of an IVF cycle. We begin by stressing the importance of enriching the standing embryo selection criteria available aiming for the golden standard: "extract as much information as possible focusing on non-invasive techniques" so as to guide us towards selecting the embryo with the highest implantation potential. We briefly describe the latest trends on how to best select the right embryo, moving closer towards elective single embryo transfer. These trends are: frozen embryo transfer for all, preimplantation genetic screening, non-invasive selection criteria, and time-lapse
imaging. The main part of this review is dedicated to categorizing and presenting published research studies focused on the involvement of CAMs in IVF and its final outcome. Specifically, we discuss the association of CAMs with conditions and complications that arise from performing assisted reproductive techniques, such as ovarian hyperstimulation syndrome, the state of the endometrium, and tubal pregnancies, as well as the levels of CAMs in biological materials available in the IVF laboratory such as follicular fluid, trophectoderm, ovarian granulosa cells, oocytes, and embryos. To conclude, since CAMs have been successfully employed as a diagnostic tool in several pathologies in routine clinical work, we suggest that their multi-faceted nature could serve as a prognostic marker in assisted reproduction, aiming to enrich the list of non-invasive selection and predictive criteria in the IVF setting. We propose that in light of the well-documented involvement of CAMs in the developmental processes of fertilization, embryogenesis, implantation, placentation, and embryonic development, further studies could contribute significantly to achieving a higher quality of treatment and management of infertility.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available In vivo (Athens, Greece) at No link? Ask Salisbury Healthcare Library - please click here to request article.

6. Cetrotide administration in the early luteal phase in patients at high risk of ovarian hyperstimulation syndrome: A controlled clinical study  
**Citation:** Experimental and Therapeutic Medicine, December 2014, vol./is. 8/6(1855-1860), 1792-0981;1792-1015 (01 Dec 2014)  
**Author(s):** Wang Y.-Q., Yu N., Xu W.-M., Xie Q.-Z., Yan W.-J., Wu G.-X., Yang J.  
**Language:** English  
**Abstract:** The aim of the present pilot study was to assess the feasibility and efficacy of Cetrotide administration in the early luteal phase in patients at high risk of ovarian hyperstimulation syndrome (OHSS), undergoing embryo cryopreservation following superovulation. A total of 135 patients at high risk of OHSS and undergoing embryo cryopreservation were divided into two groups. In the treatment group (n=39), the patients received daily subcutaneous injections of 0.25 mg Cetrotide between days 1 and 5 following oocyte retrieval, and volume expansion and symptomatic treatment were also provided. In the control group (n=96), the patients received routine treatments, including volume expansion therapy. The serum steroid hormone concentrations of the patients were measured on days 2, 5 and 8 following oocyte retrieval, while the incidence of moderate or severe OHSS, self-evaluated clinical symptoms and various clinical indicators were recorded. The serum estradiol (E2), luteinizing hormone and progesterone levels in the treatment group on days 2, 5 and 8 following oocyte retrieval were not found to differ significantly when compared with the patients in the control group (P>0.05). The incidence of severe OHSS did not differ significantly between the two groups (P>0.05). The average length of hospital stay and length of luteal phase were not found to be significantly different between the treatment and control groups (P>0.05). In conclusion, Cetrotide injections in the early luteal phase did not alter the serum steroid levels of patients at high risk of OHSS undergoing embryo cryopreservation, and were unable to reduce the incidence of severe early OHSS. However, further randomized studies are required to evaluate the effectiveness of Cetrotide in the prevention of OHSS.

**Publication type:** Journal: Article  
**Source:** EMBASE  
**Full text:** Available Experimental and Therapeutic Medicine at No link? Ask Salisbury Healthcare Library - please click here to request article.

7. Comparative evaluation of vascular endothelial growth factor-A expression in pre-ovulatory follicular fluid in normogonadotrophic and endometriotic patients undergoing assisted reproductive techniques  
**Citation:** Middle East Fertility Society Journal, December 2014, vol./is. 19/4(248-261), 1110-5690;2090-3251 (01 Dec 2014)  
**Author(s):** Orief Y.I., Karkor T.A.E., Aly Saleh H., El Hadidy A.S., Badr N.  
**Language:** English  
**Abstract:** Objective The aim of this study is to compare the differential expression of VEGF-A in pre-ovulatory follicular fluid of both normogonadotrophic and endometriotic patients undergoing ICSI and its relation to ICSI outcome. Setting Agial IVF - ICSI center, Alexandria, Egypt. Methodology The study was a prospective randomized
control trial that included 90 infertile patients who were subdivided into two groups: Group A: 45 normogonadotrophic patients as patients having tubal factor and unexplained infertility. Group B: 45 endometriotic patients diagnosed by laparoscopy. All patients underwent the same ovarian hyperstimulation protocol (the long luteal phase protocol). In all patients the blood was sampled on the day of HCG administration. The isolated sera were frozen and stored at -20 degreeC for later hormone analysis (assay of estradiol and progesterone). The follicular fluid was collected on the day of oocyte retrieval from all the patients. Only aspirates from follicles larger than 17 mm, uncontaminated with blood were included in this study. Follicular fluid samples were centrifuged for 10 min, and the supernatants were stored at -20degreeC until hormone measurements were carried out (assay of estradiol, progesterone and androstenedione). VEGF-A assay was performed using the ELISA technique for all the follicular fluid samples and the results were correlated to the ICSI outcome in both groups.

Outcome measures The primary outcome measures were: (a) The number of mature oocytes per cycle of induction, (b) the grading of embryos obtained, (c) implantation rate, (d) serum level of estradiol and progesterone on the day of HCG administration and (e) follicular fluid level of estradiol, progesterone and androstenedione on the day of oocyte retrieval. The secondary outcome measure was pregnancy rate which was diagnosed by: 1. Serum B-hCG assay 14 days after embryo transfer. 2. Clinical pregnancy rate.

Results There was a statistically significant difference between the two groups when comparing the mean value of the follicular fluid VEGF-A concentrations. In group A, the mean value was 529.4 + 309.7 (pg/ml), while in group B, it was 1388.7 + 1152 (pg/ml) (p value = 0.0001). There was no statistical significant difference between both groups as regards the outcome of pregnancy. When correlating between ICSI outcome and different studied parameters a positive correlation was detected between the ICSI outcome and endometrial thickness. No correlation could be detected between the ICSI outcome and other studied parameters. No correlations could be detected between VEGF-A expression and different studied laboratory parameters. However, a positive correlation was detected between VEGF-A and ICSI outcomes in both groups, it means that increasing the level of VEGF-A is accompanied with a decrease in the pregnancy rate (p = 0.003), a negative correlation was detected between VEGF-A and endometrial thickness, a positive correlation was detected between VEGF-A and metaphase I oocytes, otherwise no other correlations could be detected.

Conclusion The current study concluded that follicular fluid VEGF-A is correlated negatively with the ICSI outcome.

Publication type: Journal: Article
Source: EMBASE
Full text: Available Middle East Fertility Society Journal at No link? Ask Salisbury Healthcare Library - please click here to request article.

8. Dopamine agonists in prevention of ovarian hyperstimulation syndrome

Citation: Gynecological Endocrinology, December 2014, vol./is. 30/12(845-849), 0951-3590;1473-0766 (01 Dec 2014)

Author(s): Kasum M., Vrcic H., Stanic P., Jezek D., Oreskovic S., Beketic-Oreskovic L., Pekez M.

Language: English

Abstract: The aim of this review is to analyze the efficacy of different dopamine agonists in the prevention of ovarian hyperstimulation syndrome (OHSS). Cabergoline, quinagolide and bromocriptine are the most common dopamine agonists used. There are wide clinical variations among the trials in the starting time (from the day of human chorionic gonadotrophin (hCG) to the day following oocyte retrieval); the duration of the treatment (4-21 days), the dose of cabergoline (0.5mg or 0.25mg orally) and in the regimens used. At present, the best known effective regimen is 0.5mg of cabergoline for 8 days or rectal bromocriptine at a daily dose of 2.5mg for 16 days. Dopamine agonists have shown significant evidences of their efficacy in the prevention of moderate and early-onset OHSS (9.41%), compared with a placebo (21.45%), which cannot be confirmed for the treatment of late OHSS. It would be advisable to start with the treatment on the day of hCG injection or preferably a few hours earlier. The use of dopamine agonists should be indicated in patients at high risk of OHSS, as well as in patients with a history of previous OHSS even without evident signs of the syndrome.

Publication type: Journal: Article
Source: EMBASE
Full text: Available Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology at No link? Ask Salisbury Healthcare Library - please click here to request article.

9. Dual ovarian stimulation is a new viable option for enhancing the oocyte yield when the time for assisted reproductive technology is limited
Abstract: Ovarian stimulation improves assisted reproductive technology outcome by increasing the number of oocytes available for insemination and in-vitro handling. A recent Duplex protocol features a dual stimulation, with the second stimulation started immediately after the first oocyte retrieval. Remarkably, the Duplex protocol is unexpectedly well tolerated by women and provides twice as many oocytes and embryos as a regular antagonist protocol in less than 30 days.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Reproductive biomedicine online at No link? Ask Salisbury Healthcare Library - please click here to request article.

10. Effect of piroxicam on ART outcome: A pilot study
Citation: International Journal of Fertility and Sterility, October 2014, vol./is. 8/3(243-248), 2008-076X;2008-0778 (01 Oct 2014)
Author(s): Sohrabvand F., Haghollahi F., Maasomi M., Shariat M.
Language: English
Abstract: Background: One of the most important factors affecting success rates in assisted reproductive techniques (ART) besides the number of oocytes retrieved and high quality embryos derived from them is the technical aspects of embryo transfer. It seems that pretreatment with uterine relaxants can be helpful in preventing unpleasant cramps which can have an adverse effect on ART outcome. In this respect, some drugs such as prostaglandin inhibitors or sedatives have been evaluated but not confirmed yet remain controversial. This study was performed in order to assess the effect of administrating Piroxicam prior to embryo transfer on pregnancy rates in ART cycles.

Materials and Methods: This pilot study was performed from August 2010 through December 2011 on 50 infertile women in ART cycles. Recombinant follicle stimulating hormone (rFSH) with a long gonadotropin releasing hormone (GnRH) analogue protocol were used for controlled ovarian hyperstimulation. The subjects were randomly allocated into two groups of 25 patients after obtaining written consent. Group A received a 10 mg Piroxicam capsule 30 minutes before embryo transfer and group B was the control group with no treatment.

Data were analyzed by Chi-square and analysis of variance (ANOVA).

Results: Pregnancy rate was 34% (n=17) totally, with 32% (n=8) in group A and 36% (n=9) in group B (p=0.75). Uterine cramps were experienced by 4 women (16%) in group B, while none were reported by women in group A (p=0.037).

Conclusion: It seems that Piroxicam administration 30 minutes prior to embryo transfer cannot increase pregnancy rates, but can prevent or reduce uterine cramps after the procedure.

Publication type: Journal: Article
Source: EMBASE
Full text: Available International Journal of Fertility and Sterility at International Journal of Fertility and Sterility
Full text: Available International Journal of Fertility and Sterility at No link? Ask Salisbury Healthcare Library - please click here to request article.

11. Effects of different doses of letrozole on the incidence of early-onset ovarian hyperstimulation syndrome after oocyte retrieval
Citation: Systems Biology in Reproductive Medicine, December 2014, vol./is. 60/6(355-360), 1939-6368;1939-6376 (01 Dec 2014)
Author(s): He Q., Liang L., Zhang C., Li H., Ge Z., Wang L., Cui S.
Language: English
Abstract: We explored the effects of different doses of letrozole on the incidence of ovarian hyperstimulation syndrome (OHSS) after oocyte retrieval during in vitro fertilization (IVF) in patients with high-risk OHSS. A total of 88 patients were randomly divided into a control group, and groups treated with 2.5mg, 5mg, or 7.5mg of letrozole. We found that from the fifth day after human chorionic gonadotrophin (hCG) treatment, the E2 level decreased and there were statistical differences between the four groups (p<0.05). From the eighth day after hCG treatment, the luteinizing hormone (LH) level increased, but the progesterone (P) level decreased. There were statistical differences between groups (p<0.05). From the fifth day after hCG treatment, the level of vascular endothelial growth factor (VEGF) increased in the control, but decreased in the letrozole groups in a dose-
dependent manner. There were statistically significant differences between groups (p<0.001). The incidence of moderate and severe OHSS was lower in the 7.5mg group than in the control group (p<0.05). In the patients with high-risk OHSS undergoing whole embryo frozen transfer, treatment with 7.5mg letrozole may be useful to limit OHSS.

Publication type: Journal: Article
Source: EMBASE
Full text: Available Systems biology in reproductive medicine at No link? Ask Salisbury Healthcare Library - please click here to request article.

12. Effects of short-term fertilization versus conventional fertilization in vitro fertilization cycles: A meta-analysis

Citation: Chinese Journal of Evidence-Based Medicine, 2014, vol./is. 14/12(1504-1509), 1672-2531 (2014)
Author(s): Jian Q.-L., Wang F., Ding N., Du H., Huang S.
Language: Chinese
Abstract: Objective To systematically review the clinical effects of short-term and conventional fertilization for vitro fertilization-embryo transfer (IVF-ET). Methods Randomized controlled trials (RCTs) about the clinical effects of short-term fertilization versus conventional fertilization for IVF-ET were searched in PubMed, Te Cochrane Library (Issue 8, 2014), CBM, CNKI, WanFang Data and VIP from inception to August 2014. Two reviewers independently screened literature according to the inclusion and exclusion criteria, extracted data, and assessed methodological quality of included studies. Then meta-analysis was performed using RevMan 5.2 software. Results A total of six RCTs involving 1 373 patients were finally included. Te results of meta-analysis indicated that: short-term fertilization was superior to conventional fertilization in increasing high quality embryo rates (OR=1.42, 95%CI 1.18 to 1.70, P=0.000 2) as well as clinical pregnancy rates (OR=1.67, 95%CI 1.33 to 2.09, P<0.000 01). However, the two groups were alike in fertilization rates, polyspermy rates, and miscarriage rates. Conclusion Current evidence indicates that short-term fertilization is superior to conventional fertilization in increasing high quality embryo rates as well as clinical pregnancy rates. Due to limited quality and quantity of the included studies, the above conclusion should be verified by conducting more large-scale, high quality RCTs with long-term follow-up.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Chinese Journal of Evidence-Based Medicine at No link? Ask Salisbury Healthcare Library - please click here to request article.

13. Fresh versus frozen embryo transfer: Backing clinical decisions with scientific and clinical evidence

Citation: Human Reproduction Update, November 2014, vol./is. 20/6(808-821), 1355-4786;1460-2369 (01 Nov 2014)
Language: English
Abstract: Background: Improvements in vitrification now make frozen embryo transfers (FETs) a viable alternative to fresh embryo transfer, with reports fromobservational studies and randomized controlled trials suggesting that: (i) the endometrium in stimulated cycles is not optimally prepared for implantation; (ii) pregnancy rates are increased following FET and (iii) perinatal outcomes are less affected after FET. methods: This review integrates and discusses the available clinical and scientific evidence supporting embryo transfer in a natural cycle. results: Laboratory-based studies demonstrate morphological and molecular changes to the endometrium and reduced responsiveness of the endometriumtohCG, resulting fromcontrolledovarian stimulation. Theliteraturedemonstrates reducedendometrial receptivity incontrolledovarian stimulation cycles and supports the clinical observations that FET reduces the risk of ovarian hyperstimulation syndrome and improves outcomes for both the mother and baby. conclusions: This review provides the basis for an evidence-based approach towards changes in routine IVF, which may ultimately result in higher delivery rates of healthier term babies.

Publication type: Journal: Article
Source: EMBASE
Full text: Available Human reproduction update at No link? Ask Salisbury Healthcare Library - please click here to
14. GnRH agonist trigger and a freeze-all strategy to prevent ovarian hyperstimulation syndrome: A retrospective study of OHSS risk and pregnancy rates

**Citation:** Australian and New Zealand Journal of Obstetrics and Gynaecology, December 2014, vol./is. 54/6(581-585), 0004-8666;1479-828X (01 Dec 2014)

**Author(s):** Atkinson P., Koch J., Ledger W.L.

**Language:** English

**Abstract:** Aims To analyse the data from all controlled ovarian hyperstimulation antagonist cycles that used an agonist trigger and a freeze-all strategy to quantify the risk of ovarian hyperstimulation syndrome (OHSS) and subsequent pregnancy rates. Materials and Methods A retrospective study of all women attending fertility clinics at IVF Australia, Sydney, undergoing controlled ovarian hyperstimulation (COH) using an antagonist protocol that had a subsequent gonadotropin-releasing hormone (GnRH) agonist trigger and freezing of all oocytes or embryos. The primary outcome measure was to determine the rate of OHSS. The secondary outcome measure was the clinical pregnancy rate. Results We collected data for 123 women. 25.2% were undergoing oocyte freezing and 74.8% underwent embryo freezing. There were no cases of OHSS, either early or late onset. The pregnancy rate was 31.7% after the first frozen cycle transfer with a cumulative pregnancy rate of 50% after two frozen embryo transfers. Conclusion Our results support the hypothesis that a GnRH agonist trigger and a freeze-all approach prevents OHSS with a good pregnancy rate.

**Publication type:** Journal: Article

**Source:** EMBASE

**Full text:** Available Australian & New Zealand Journal of Obstetrics & Gynaecology at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

15. Gonadotrophin-releasing hormone agonist trigger and freeze-all strategy does not prevent severe ovarian hyperstimulation syndrome: A report of three cases

**Citation:** Reproductive BioMedicine Online, November 2014, vol./is. 29/5(541-544), 1472-6483;1472-6491 (01 Nov 2014)

**Author(s):** Gurbuz A.S., Gode F., Ozcimen N., Isik A.Z.

**Language:** English

**Abstract:** Ovarian hyperstimulation syndrome (OHSS) is the most serious iatrogenic complication of IVF cycles. Although the development of effective treatment strategies for this syndrome is important, preventing OHSS is more crucial. Triggering ovulation with a gonadotrophin-releasing hormone (GnRH) agonist is one method used to avoid OHSS. In this paper, three patients who developed severe OHSS after undergoing GnRH agonist triggering and freezing of all embryos in a GnRH antagonist protocol are described. A review of the literature is also provided. This report highlights the ongoing risk of severe OHSS even after GnRH agonist triggering combined with freezing all embryos in GnRH antagonist cycles. Other prevention strategies might be considered for extreme hyper-responders.

**Publication type:** Journal: Article

**Source:** EMBASE

**Full text:** Available Reproductive biomedicine online at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

16. Health and disease in children born after assistive reproductive therapies (ART)

**Citation:** Journal of Reproductive Immunology, December 2014, vol./is. 106/(21-26), 0165-0378;1872-7603 (01 Dec 2014)

**Author(s):** Hyrapetian M., Loucaides E.M., Sutcliffe A.G.

**Language:** English

**Abstract:** In vitro fertilisation (IVF) and other assisted reproductive therapies (ART) offer hope to subfertile couples worldwide. At least 5 million ART children have been born to date. Their health is an issue that is increasingly relevant: first, to those children and young adults themselves; second, to couples considering fertility treatment; and third, to the general population as ART has progressed from experimental treatment to routine practice. Many concerns about the potential risks to these children have been voiced with varying degrees of supportive evidence. This article summarises some key long-term data. Current evidence suggests that ART does...
increase risk of: higher order pregnancy (with its inherent pre- and perinatal risks); prematurity and low birth weight; congenital malformations in particular of the male urogenital system; imprinting disorders. Reassuringly, evidence points away from an increased overall cancer risk or differences in neurodevelopmental outcomes. Many unknowns remain, including future fertility and cardiovascular risks and risk of cerebral palsy.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Journal of reproductive immunology at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

17. Improved cycle outcomes after laparoscopic ovarian diathermy in hyper-responder patients with previous ART failure  
**Citation:** Gynecological Endocrinology, December 2014, vol./is. 30/12(881-884), 0951-3590;1473-0766 (01 Dec 2014)  
**Author(s):** Pabuccu R., Pabuccu E.G., Gursoy A.Y., Caglar G.S., Yilmaz M.B., Ozdegirmenci O.  
**Language:** English  
**Abstract:** Excessive response to ovarian stimulation is common among hyper-responder patients undergoing assisted reproductive technology (ART). Cycle cancellations and severe ovarian hyperstimulation syndrome (OHSS) are all detrimental consequences observed within this cohort and several approaches have been proposed to enhance outcomes. The current study is designed to evaluate whether laparoscopic ovarian diathermy (LOD) improves ART outcomes and pregnancy rates by reducing Anti-mullerian hormone (AMH) levels in a group of patients who had a history of recurrent ART failure and high response. A total of 40 hyper-responder patients with history of previous ART failure were included. Group I consisted of 22 patients that underwent LOD prior to ART. Group II consisted of 18 patients that underwent only ART. Cycle outcomes of groups were compared. Following LOD, significant reduction in AMH levels were detected in group I (4.75ng/mL to 2.25ng/mL). Clinical pregnancies were similar among groups (40% versus 27.8% p=0.65). There was no cycle cancellation in Group I, whereas there were three cycle cancellations observed due to OHSS in Group II. Our results indicate that LOD might offer enhanced fertility outcomes and may reduce the likelihood of cycle cancellations in hyper-responders with previous ART failures.

**Publication type:** Journal: Article  
**Source:** EMBASE  
**Full text:** Available Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

**Citation:** Obstetrics & Gynecology, January 2015, vol./is. 125/1(79-88), 0029-7844;1873-233X (2015 Jan)  
**Author(s):** Hamdan M, Omar SZ, Dunselman G, Cheong Y  
**Language:** English  
**Abstract:** OBJECTIVE: To investigate the association of endometriosis on assisted reproductive technology (ART) outcomes and to review if surgical treatment of endometriosis before ART affects the outcomes.DATA SOURCES: We searched studies published between 1980 and 2014 on endometriosis and ART outcome. We searched MEDLINE, PubMed, ClinicalTrials.gov, and Cochrane databases and performed a manual search.METHODS OF STUDY SELECTION: A total of 1,346 articles were identified, and 36 studies were eligible to be included for data synthesis. We included published cohort studies and randomized controlled trials.TABULATION, INTEGRATION, AND RESULTS: Compared with women without endometriosis, women with endometriosis undertaking in vitro fertilization and intracytoplasmic sperm injection have a similar live birth rate per woman (odds ratio [OR] 0.94, 95% confidence interval [CI] 0.84-1.06, 13 studies, 12,682 patients, I=35%), a lower clinical pregnancy rate per woman (OR 0.78, 95% CI 0.65-0.94), 24 studies, 20,757 patients, I=66%), a lower mean number of oocyte retrieved per cycle (mean difference -1.98, 95% CI -2.87 to -1.09, 17 studies, 17,593 cycles, I=97%), and a similar miscarriage rate per woman (OR 1.26, 95% CI (0.92-1.70, nine studies, 1,259 patients, I=0%). Women with more severe disease (American Society for Reproductive Medicine III-IV) have a lower live birth rate, clinical pregnancy rate, and mean number of oocytes retrieved when compared with women with no endometriosis.CONCLUSION: Women with and without endometriosis have comparable ART outcomes in terms of live births, whereas those with severe endometriosis have inferior outcomes. There is insufficient evidence to recommend surgery routinely before undergoing ART.
19. In-vitro maturation versus IVF with GnRH antagonist for women with polycystic ovary syndrome: Treatment outcome and rates of ovarian hyperstimulation syndrome

Citation: Reproductive BioMedicine Online, November 2014, vol./is. 29/5(545-551), 1472-6483;1472-6491 (01 Nov 2014)

Author(s): Das M., Son W.-Y., Buckett W., Tulandi T., Holzer H.

Language: English

Abstract: In-vitro maturation (IVM) treatment has gained popularity for decreasing the incidence of ovarian hyperstimulation syndrome (OHSS) by eliminating or minimizing the use of gonadotrophins in women with polycystic ovary syndrome (PCOS). Studies have shown that IVF with GnRH-antagonist protocol is associated with a lower incidence of OHSS. Data comparing the relative success of these two treatments is, however, lacking. Treatment outcome and rates of OHSS were compared in patients with PCOS who underwent assisted conception with either IVM or IVF with GnRH-antagonist protocol between 2006 and 2011. The number of oocytes retrieved was higher in the IVM group, whereas the number of mature oocytes, fertilization rate and number of embryos cleaved were comparable. The implantation rate was higher in the IVF group. The clinical pregnancy rates per embryo transfer were not statistically different (IVF: 45.8% versus IVM: 32.4%). The live-birth rate was higher in the IVF group (IVF: 40.7% versus IVM: 23.5%; P = 0.04). Five women developed moderate or severe OHSS in the IVF group, whereas none did in the IVM group. Both IVM and IVF with GnRH-antagonist protocol seem to be effective treatment regimens in women with PCOS, although IVM is associated with a lower risk of OHSS.

20. Metformin in reproductive health, pregnancy and gynaecological cancer: Established and emerging indications

Citation: Human Reproduction Update, November 2014, vol./is. 20/6(853-868), 1355-4786;1460-2369 (01 Nov 2014)

Author(s): Sivalingam V.N., Myers J., Nicholas S., Balen A.H., Crosbie E.J.

Language: English

Abstract: Background: Metformin is an effective oral anti-hyperglycaemic drug used as first-line medical treatment for type 2 diabetes. It improves systemic hyperglycaemia by reducing hepatic glucose production and enhancing peripheral insulin sensitivity. It also stimulates fat oxidation and reduces fat synthesis and storage. The molecular mechanism of this drug is thought to be secondary to its actions on the mitochondrial respiratory chain. Methods: This paper reviews the relevant literature (research articles up to October 2013) on the use of metformin in infertility, polycystic ovary syndrome (PCOS), pregnancy and gynaecological cancers. We present a comprehensive discussion of the evidence supporting the efficacy of metformin in these clinical conditions. Result: Metformin is used clinically off-label in the management of hirsutism, acne and insulin resistance in PCOS, although the evidence for anti-androgenic effects is inconsistent. Metformin is also used to improve ovulation in women with PCOS both alone and in combination with clomiphene citrate. Trial findings are conflicting but metformin treatment in IVF/ICSI cycles may reduce the risk of ovarian hyperstimulation syndrome and increase live birth rates. Metformin also appears to be effective and safe for the treatment of gestational diabetes mellitus (GDM), particularly for overweight and obese women. Studies have shown that metformin is safe in pregnancy and women with GDM treated with metformin have less weight gain during pregnancy than those treated with insulin. One study with a 2-year follow-up demonstrated that babies born to women treated with metformin also developed less visceral fat, making them less prone to insulin resistance in later life. These findings have sparked interest in the use of metformin for pregnant, obese, non-diabetic women. On-going clinical trials are underway to determine if women treated prophylactically with metformin have a reduced incidence of GDM and demonstrate less weight gain during pregnancy. The hypothesis in these studies is that babies born to obese women on prophylactic metformin will also have better outcomes. Epidemiological studies have linked metformin exposure to a decreased risk of cancer. Pre-clinical experiments report that metformin has a growth-static effect on several cancers, including endometrial cancer, which may be partly due to the effect of metformin on the
PI3K/AKT/mTOR signal transduction pathway. A number of on-going early phase clinical trials aim to explore the anti-cancer effects of metformin and investigate its potential as a chemopreventative or adjuvant treatment. Conclusions: Obesity is on the rise in developing countries and is strongly linked to several reproductive health problems, including PCOS, GDM and endometrial cancer. Traditional lifestyle measures aimed at weight reduction are challenging to implement and maintain. Metformin may be a valuable alternative to, or adjunct for, modifying the toxic effects of obesity in these populations. This review will appraise the evidence for the use of metformin for the prevention and treatment of adverse health outcomes in obstetrics and gynaecology.

**Publication type:** Journal: Article  
**Source:** EMBASE  
**Full text:** Available Human reproduction update at No link? Ask Salisbury Healthcare Library - please click here to request article.

21. Oocyte versus embryo vitrification for delayed embryo transfer: An observational study

**Citation:** Reproductive BioMedicine Online, November 2014, vol./is. 29/5(567-572), 1472-6483;1472-6491 (01 Nov 2014)  
**Author(s):** Grassa L.H., Marin S.P., Barragan M.A., Cobo A., Campos F.B., Garcia-Velasco J.A.  
**Language:** English  
**Abstract:** The aim of this observational prospective study was to compare multiple embryological and pregnancy outcomes for vitrified oocytes against the same outcomes using vitrified embryos in patients at risk for ovarian hyperstimulation syndrome. Ninety-six patients were included and allocated to vitrification of oocytes (Group 1) or embryos (Group 2). No statistical differences in baseline characteristics between groups were detected. Implantation rate was 30.6% versus 33.1%, and clinical pregnancy rate was 41.9% versus 7.1% in groups 1 and 2, respectively. A higher clinical spontaneous abortion rate occurred in group 2 (9.7% versus 21.9% for groups 1 and 2, respectively), but the same cumulative clinical pregnancy rate was observed after three embryo transfers (62.0% in group 1 and 69.6% in group 2). The ongoing pregnancy rate per patient was similar in both groups (56.0% and 54.3% in groups 1 and 2, respectively). Also, live birth rate per stimulation was similar (72.0% and 69.6% in groups 1 and 2, respectively). No differences were observed in outcomes according to vitrification timing. Oocyte vitrification achieved the same live birth rate as embryo vitrification.  
**Publication type:** Journal: Article  
**Source:** EMBASE  
**Full text:** Available Reproductive biomedicine online at No link? Ask Salisbury Healthcare Library - please click here to request article.

22. Risk of thrombosis in women with malignancies undergoing ovarian stimulation for fertility preservation

**Citation:** Human Reproduction Update, November 2014, vol./is. 20/6(944-951), 1355-4786;1460-2369 (01 Nov 2014)  
**Author(s):** Somigliana E., Peccatori F.A., Filippi F., Martinelli F., Raspagliesi F., Martinelli I.  
**Language:** English  
**Abstract:** Background: Compared with the general population, cancer patients have a higher risk of venous thromboembolism as well as arterial thrombotic events such as stroke, myocardial infarction and peripheral arterial embolism. Therefore a possible concern for women with malignancies undergoing ovarian stimulation for fertility preservation is the increased risk of venous or arterial thrombosis. Methods: In this article, we revised current available literature on the risk of thrombosis in patients with cancer and in women undergoing ovarian stimulation, with the ultimate aim of drawing some indications for preventive measures. Results: Unfortunately, there are no specific data on the risk of thrombosis in women with cancer undergoing ovarian stimulation for fertility preservation. However, the literature suggests that the cancer type and stage, surgery, and chemotherapy all influence the risk of venous and, possibly, arterial thrombosis. Reports of cases of ovarian stimulation in women without malignancies have shown that venous thrombosis rarely occurs unless a pregnancy is achieved, while arterial thrombosis can occur in the absence of pregnancy but is usually only associated with ovarian hyperstimulation syndrome (OHSS). OHSS increases the risk of thrombotic events, but only the early form of the syndrome is relevant for women undergoing fertility preservation. Conclusions: The available evidence on the risks of thrombosis for women undergoing ovarian stimulation for fertility preservation due to a malignancy is reassuring. However the avoidance of the early form of OHSS in women preserving oocytes/embryos due to malignancy is crucial. For these cycles, we advocate the use of a regimen of ovarian stimulation with
gonadotrophin releasing hormone (GnRH) antagonists using GnRH agonists to trigger ovulation, an approach that has been shown to markedly reduce the risk of OHSS. Antithrombotic prophylaxis should be administered only to selected subgroups of women such as those with other risk factors or those who do develop early OHSS.

**Publication type:** Journal: Article  
**Source:** EMBASE  
**Full text:** Available *Human reproduction update* at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

### 23. The luteal phase after GnRHa trigger-understanding an enigma

**Citation:** International Journal of Fertility and Sterility, October 2014, vol./is. 8/3(227-234), 2008-076X;2008-0778 (01 Oct 2014)  
**Author(s):** Leth-Moller K., Jagd S.H., Humaidan P.  
**Language:** English  
**Abstract:** The luteal phase of all stimulated in vitro fertilization/intra-cytoplasmonic sperm injection (IVF/ICSI) cycles is disrupted, which makes luteal phase support (LPS) mandatory. The cause of the disruption is thought to be the multifollicular development achieved during ovarian stimulation which results in supraphysiological concentrations of steroids secreted by a high number of corpora lutea during the early luteal phase. This will directly inhibit luteinizing hormone (LH) secretion by the pituitary via negative feedback at the level of the hypothalamic-pituitary axis, leading to a luteal phase defect. With the introduction of the gonadotropin-releasing hormone (GnRH) antagonist protocol, it became feasible to trigger final oocyte maturation and ovulation with a single bolus of GnRH agonist (GnRHa) as an alternative to human chorionic gonadotropin (hCG). GnRHa triggering presents several advantages, including the reduction in or even elimination of ovarian hyperstimulation syndrome. Despite the potential advantages of GnRHa triggering, previous randomized controlled trials reported a poor clinical outcome with high rates of early pregnancy losses, despite supplementation with a standard LPS in the form of progesterone and estradiol. Following these disappointing results, several studies now report a luteal phase rescue after modifications of the LPS, resulting in a reproductive outcome comparable to that seen after hCG triggering. We herein review luteal phase differences between the natural cycle, hCG trigger and GnRHa trigger and present the most recent data on handling the luteal phase after GnRHa triggering.

**Publication type:** Journal: Article  
**Source:** EMBASE  
**Full text:** Available *International Journal of Fertility and Sterility* at [International Journal of Fertility and Sterility](#)  
**Full text:** Available *International Journal of Fertility and Sterility* at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

### 24. The role of selenium in human conception and pregnancy

**Citation:** Journal of Trace Elements in Medicine and Biology, January 2015, vol./is. 29/(31-38), 0946-672X;1878-3252 (01 Jan 2015)  
**Author(s):** Pieczymska J., Grajeta H.  
**Language:** English  
**Abstract:** Selenium (Se) is a trace element essential for the appropriate course of vital processes in the human body. It is also a constituent of the active center of glutathione peroxidase that protects cellular membranes against the adverse effects of $H_2O_2$ lipid peroxides. Epidemiological surveys have demonstrated that selenium deficiency in the body may contribute to an increased risk for certain neoplastic diseases (including colonic carcinoma, gastric carcinoma, pulmonary carcinoma and prostate carcinoma), as well as diseases of the cardiovascular, osseous and nervous systems. Apart from its cancer prevention and antioxidative activities, selenium protects the body against detrimental effects of heavy metals and determines the proper functioning of the immunological system. Furthermore, selenium plays a significant role in the undisturbed functioning of the reproductive system. Many studies have addressed correlations between its intake and fertility as well as disorders of procreation processes. Selenium deficiencies may lead to gestational complications, miscarriages and the damaging of the nervous and immune systems of the fetus. A low concentration of selenium in blood serum in the early stage of pregnancy has been proved to be a predictor of low birth weight of a newborn. A deficiency of this element may also cause infertility in men by causing a deterioration in the quality of semen and in sperm motility. For this reason, supplementation in the case of selenium deficiencies in the procreation period of both women and men is of utmost significance.

**Publication type:** Journal: Review
25. Risk of thrombosis in women with malignancies undergoing ovarian stimulation for fertility preservation

Citation: Human Reproduction Update, November 2014, vol./is. 20/6(944-951), 1355-4786;1460-2369 (01 Nov 2014)

Author(s): Somigliana E., Peccatori F.A., Filippi F., Martinelli F., Raspagliesi F., Martinelli I.

Language: English

Abstract: Background: Compared with the general population, cancer patients have a higher risk of venous thromboembolism as well as arterial thrombotic events such as stroke, myocardial infarction and peripheral arterial embolism. Therefore a possible concern for women with malignancies undergoing ovarian stimulation for fertility preservation is the increased risk of venous or arterial thrombosis. Methods: In this article, we revised current available literature on the risk of thrombosis in patients with cancer and in women undergoing ovarian stimulation, with the ultimate aim of drawing some indications for preventive measures. Results: Unfortunately, there are no specific data on the risk of thrombosis in women with cancer undergoing ovarian stimulation for fertility preservation. However, the literature suggests that the cancer type and stage, surgery, and chemotherapy all influence the risk of venous and, possibly, arterial thrombosis. Reports of cases of ovarian stimulation in women without malignancies have shown that venous thrombosis rarely occurs unless a pregnancy is achieved, while arterial thrombosis can occur in the absence of pregnancy but is usually only associated with ovarian hyperstimulation syndrome (OHSS). OHSS increases the risk of thrombotic events, but only the early form of the syndrome is relevant for women undergoing fertility preservation. Conclusions: The available evidence on the risks of thrombosis for women undergoing ovarian stimulation for fertility preservation due to a malignancy is reassuring. However the avoidance of the early form of OHSS in women preserving oocytes/embryos due to malignancy is crucial. For these cycles, we advocate the use of a regimen of ovarian stimulation with gonadotrophin releasing hormone (GnRH) antagonists using GnRH agonists to trigger ovulation, an approach that has been shown markedly reduce the risk of OHSS. Antithrombotic prophylaxis should be administered only to selected subgroups of women such as those with other risk factors or those who do develop early OHSS.

Publication type: Journal: Article

Source: EMBASE

Full text: Available Human reproduction update at No link? Ask Salisbury Healthcare Library - please click here to request article.


Citation: Human Reproduction Update, November 2014, vol./is. 20/6(869-83), 1355-4786;1460-2369 (2014 Nov-Dec)

Author(s): Persani L, Rossetti R, Di Pasquale E, Cacciatore C, Fabre S

Language: English

Abstract: BACKGROUND: A large number of studies have contributed to understanding the general mechanisms driving ovarian folliculogenesis in humans and show a complex endocrine dialog between the central nervous system, the pituitary and the ovary, integrated by various intraovarian paracrine messages. The role of intraovarian paracrine regulation has acquired more relevance in the recent years owing to the discovery of previously unknown factors, such as the oocyte-derived bone morphogenetic protein (BMP)15. METHODS: A thorough literature search was carried out in order to summarize what has been reported so far on the role of BMP15, and the BMP15 paralog, growth and differentiation factor 9 (GDF9), in ovarian function and female fertility. Research articles published in English until March 2014 were included. RESULTS: The biological actions of BMP15 include: (i) the promotion of follicle growth and maturation starting from the primary gonadotrophin-independent phases of folliculogenesis; (ii) the regulation of follicular granulosa cell (GC) sensitivity to FSH action and the determination of ovulation quota; (iii) the prevention of GC apoptosis and (iv) the promotion of oocyte developmental competence. The existence of biologically active heterodimers with GDF9, and/or the synergistic co-operation of BMP15 and GDF9 homodimers are indeed relevant in this context. Experimental disruption of thebmp15 gene in mice resulted in a mild fertility defect limited to females, whereas natural missense mutations in ewes cause variable phenotypes (ranging from hyperprolificacy to complete sterility) depending on a fine gene
dosage mechanism also involving GDF9. Strong evidence supports the concept that such a mechanism plays an important role in the regulation of ovulation rate across mammalian and non-mammalian species. Following the discovery of sheep fecundity genes, several research groups have focused on alterations in human BMP15 associated with primary ovarian insufficiency (POI) or polycystic ovary syndrome. Several variants of BMP15 are significantly associated with POI supporting their pathogenic role, but the underlying biological mechanism is still under investigation and of great interest in medicine. BMP15 maps to the Xp locus involved in the determination of the ovarian defect in Turner syndrome and significantly contributes to the determination of ovarian reserve. Pioneering studies in women undergoing controlled ovarian stimulation indicate that BMP15 may represent a marker of ovarian response or oocyte quality.

CONCLUSIONS: BMP15, an oocyte-derived growth and differentiation factor, is a critical regulator of folliculogenesis and GC activities. Variations in BMP15 gene dosage have a relevant influence on ovarian function and can account for several defects of female fertility. The modulation of BMP15 action may have interesting pharmacological perspectives and the analysis of BMP15 may become a useful marker in IVF procedures. Recent outcomes indicate that the close interactions of BMP15/GDF9 have a critical biological impact that should be taken into account in future studies.

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

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27. The luteal phase after GnRHa trigger—understanding an enigma

**Citation:** International Journal of Fertility and Sterility, October 2014, vol./is. 8/3(227-234), 2008-076X;2008-0778 (01 Oct 2014)

**Author(s):** Leth-Moller K., Jagd S.H., Humaidan P.

**Language:** English

**Abstract:** The luteal phase of all stimulated in vitro fertilization/intra-cytoplasmic sperm injection (IVF/ICSI) cycles is disrupted, which makes luteal phase support (LPS) mandatory. The cause of the disruption is thought to be the multifollicular development achieved during ovarian stimulation which results in supraphysiological concentrations of steroids secreted by a high number of corpora lutea during the early luteal phase. This will directly inhibit luteinizing hormone (LH) secretion by the pituitary via negative feedback at the level of the hypothalamic-pituitary axis, leading to a luteal phase defect. With the introduction of the gonadotropin-releasing hormone (GnRH) antagonist protocol, it became feasible to trigger final oocyte maturation and ovulation with a single bolus of GnRH agonist (GnRHa) as an alternative to human chorionic gonadotropin (hCG). GnRHa triggering presents several advantages, including the reduction in or even elimination of ovarian hyperstimulation syndrome. Despite the potential advantages of GnRHa triggering, previous randomized controlled trials reported a poor clinical outcome with high rates of early pregnancy losses, despite supplementation with a standard LPS in the form of progesterone and estradiol. Following these disappointing results, several studies now report a luteal phase rescue after modifications of the LPS, resulting in a reproductive outcome comparable to that seen after hCG triggering. We herein review luteal phase differences between the natural cycle, hCG trigger and GnRHa trigger and present the most recent data on handling the luteal phase after GnRHa triggering.

**Publication type:** Journal: Article

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**Full text:** Available [International Journal of Fertility and Sterility](#) at International Journal of Fertility and Sterility

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28. The role of selenium in human conception and pregnancy

**Citation:** Journal of Trace Elements in Medicine and Biology, January 2015, vol./is. 29/(31-38), 0946-672X;1878-3252 (01 Jan 2015)

**Author(s):** Pieczynska J., Grajeta H.

**Language:** English

**Abstract:** Selenium (Se) is a trace element essential for the appropriate course of vital processes in the human body. It is also a constituent of the active center of glutathione peroxidase that protects cellular membranes against the adverse effects of H<sub>2</sub>O<sub>2</sub> lipid peroxides. Epidemiological surveys have demonstrated that
selenium deficiency in the body may contribute to an increased risk for certain neoplastic diseases (including colonic carcinoma, gastric carcinoma, pulmonary carcinoma and prostate carcinoma), as well as diseases of the cardiovascular, osseous and nervous systems. Apart from its cancer prevention and antioxidative activities, selenium protects the body against detrimental effects of heavy metals and determines the proper functioning of the immunological system. Furthermore, selenium plays a significant role in the undisturbed functioning of the reproductive system. Many studies have addressed correlations between its intake and fertility as well as disorders of procreation processes. Selenium deficiencies may lead to gestational complications, miscarriages and the damaging of the nervous and immune systems of the fetus. A low concentration of selenium in blood serum in the early stage of pregnancy has been proved to be a predictor of low birth weight of a newborn. A deficiency of this element may also cause infertility in men by causing a deterioration in the quality of semen and in sperm motility. For this reason, supplementation in the case of selenium deficiencies in the procreation period of both women and men is of utmost significance.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)* at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

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