Healthcare Library
Current Awareness Bulletin – Fertility
October & November 2014

This monthly Current Awareness Bulletin is produced by the Healthcare Library to provide Salisbury NHS Foundation Trust staff working in Fertility Services with a range of resources to support practice. It includes recently published guidelines and research articles, news and policy items, and details of forthcoming events and conferences.

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**News**

[UpToDate®]

**What’s New in Female Reproduction**

**What’s New in Male Reproduction**

**NHS Choices**

**Moderate regular drinking may 'damage sperm'**
Friday 3rd October 2014

“Just five alcoholic drinks a week could reduce sperm quality,” The Guardian reports. A study involving Danish military recruits found that even moderate drinking, if done regularly, was associated with a drop in quality.

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**Guidelines**

National Institute for Health and Care Excellence (NICE)

**Fertility problems (QS73)**

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**Cochrane Systematic Reviews**

**New Reviews – October 2014**

**Advanced sperm selection techniques for assisted reproduction**

**Vasodilators for women undergoing fertility treatment**

**Updated Reviews – October 2014**
Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology

New Reviews – September 2014
Vitrification versus slow freezing for women undergoing oocyte cryopreservation

Journals – latest issue with full text access

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

Journal Articles

Please click on the blue link at the end of the abstract (where available) to access full text. You may need an Athens username and password. To register for an Athens account click here. If you have any difficulty accessing the full text articles, or if you would like us to obtain any of the articles for you, please contact the Healthcare Library.

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**Journal articles**

1. **Adherence compounds in embryo transfer media for assisted reproductive technologies**
   **Citation:** The Cochrane database of systematic reviews, 2014, vol./is. 2/(CD007421), 1469-493X (2014)
   **Author(s):** Bontekoe S., Heineman M.J., Johnson N., Blake D.
   **Language:** English
   **Abstract:** This is an update of a Cochrane review first published in The Cochrane Library (2010, Issue 7). To increase the success rate of assisted reproductive technologies (ART), adherence compounds such as hyaluronic acid (HA) and fibrin sealant have been introduced into subfertility management. Adherence compounds are added to the embryo transfer medium to increase the likelihood of embryo implantation, with the potential for higher clinical pregnancy and live birth rates. To determine whether embryo transfer media containing adherence...
compounds improved live birth and pregnancy rates in ART cycles. The Menstrual Disorders and Subfertility Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) and MEDLINE, EMBASE and PsycINFO electronic databases were searched (up to 13 November 2013) to look for publications that described randomised controlled trials on the addition of adherence compounds to embryo transfer media. Furthermore, reference lists of all obtained studies were checked, and conference abstracts were handsearched. Only truly randomised controlled trials comparing embryo transfer media containing functional (e.g. 0.5 mg/ml HA) concentrations of adherence compounds versus transfer media containing low or no concentrations of adherence compounds were included. The adherence compounds that were identified for evaluation were HA and fibrin sealant. Two review authors selected trials for inclusion according to the above criteria, after which two review authors independently extracted the data for subsequent analysis. Statistical analysis was performed in accordance with the guidelines developed by The Cochrane Collaboration. Seventeen studies with a total of 3898 participants were analysed. One studied fibrin sealant, and the other 16 studied HA. No evidence was found of a treatment effect of fibrin sealant as an adherence compound. For HA, evidence of a positive treatment effect was identified in the six trials that reported live birth rates (odds ratio (OR) 1.41, 95% confidence interval (CI) 1.17 to 1.69; six RCTs, N = 1950, I(2) = 0%, moderate-quality evidence). Furthermore, the 14 trials reporting clinical pregnancy rates showed evidence of treatment benefit when embryos were transferred in media containing functional concentrations of HA (OR 1.39, 95% CI 1.21 to 1.60; 14 RCTs, N = 3452, I(2) = 46%, moderate-quality evidence) as compared with low or no use of HA. The multiple pregnancy rate (OR 1.86, 95% CI 1.49 to 2.31; five RCTs, N = 1951, I(2) = 0%, moderate-quality evidence) was significantly increased in the high HA group, but no significant differences in adverse event rates were found (OR 0.74, 95% CI 0.49 to 1.12; four RCTs, N = 1525, I(2) = 0%, moderate-quality evidence). Evidence suggests improved clinical pregnancy and live birth rates with the use of functional concentrations of HA as an adherence compound in ART cycles. However, the evidence obtained is of moderate quality. The increase in multiple pregnancy rate may be the result of use of a combination of an adherence compound and a policy of transferring more than one embryo. Further studies of adherence compounds with single embryo transfer need to be undertaken. 

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Wiley at [Cochrane Library, The](https://cochranelibrary.co.uk)

2. AMH: An ovarian reserve biomarker in assisted reproduction  
**Citation:** Clinica Chimica Acta, November 2014, vol./is. 437/(175-182), 0009-8981;1873-3492 (01 Nov 2014)  
**Author(s):** Peluso C., Fonseca F.L.A., Rodart I.F., Cavalcanti V., Gastaldo G., Christofolini D.M., Barbosa C.P., Bianco B.  
**Language:** English  
**Abstract:** Ovarian reserve tests provide knowledge of a possible response to controlled ovarian hyperstimulation in patients undergoing assisted reproduction treatment, allowing management and alteration of treatment protocol with the appropriate dose of gonadotrophin. Several parameters have been used as predictors of ovarian response. The basal FSH serum level on the third day of the menstrual cycle seemed to be the best predictor, but with significant intraindividual variability from one cycle to another. Thus, the anti-Mullerian hormone (AMH) emerges as a new ovarian test marker. AMH is produced exclusively in the gonads, by the granulosa cells, and plays an important role in folliculogenesis, acting on the modulation of follicular recruitment in the granulosa cells in order to limit the number of recruited oocytes and to regulate the number of growing follicles and their selection for ovulation. It has been suggested that AMH is strongly associated with oocyte yield after ovarian stimulation and could therefore be capable of predicting the ovarian response and the quality of oocytes and embryos. In this review, we discuss the role of AMH in assisted reproduction outcomes. 2013 Elsevier B.V.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Elsevier at [No link? Ask Salisbury Healthcare Library - please click here to request article.](http://example.com)  
**Full text:** Available Elsevier at Clinica Chimica Acta

3. Anti-Mullerian hormone: Ovarian reserve testing and its potential clinical implications  
**Citation:** Human Reproduction Update, September 2014, vol./is. 20/5(688-701), 1355-4786;1460-2369 (September 2014)  
**Author(s):** Broer S.L., Broekmans F.J.M., Laven J.S.E., Fauser B.C.J.M.
Aromatase inhibitors for subfertile women with polycystic ovary syndrome

Citation: The Cochrane database of systematic reviews, 2014, vol./is. 2/(CD010287), 1469-493X (2014)

Author(s): Franki S., Kremer J.A., Nelen W.L., Farquhar C.

Abstract: Polycystic ovary syndrome (PCOS) is the most common cause of infrequent periods (oligomenorrhoea) and absence of periods (amenorrhoea). It affects about 4% to 8% of women worldwide and often leads to anovulatory subfertility. Aromatase inhibitors (AIs) are a novel class of drugs that were introduced for ovulation induction in 2001. Over the last ten years clinical trials have reached differing conclusions as to whether the AI letrozole is at least as effective as the first-line treatment clomiphene citrate (CC). To evaluate the effectiveness and safety of aromatase inhibitors for subfertile women with anovulatory PCOS. We searched the following sources from inception to 24/10/2013 to identify relevant randomised controlled trials (RCTs): the Menstrual Disorders and Subfertility Group Specialised Register, the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO, Pubmed, LILACS, Web of Knowledge, the World Health Organisation (WHO) clinical trials register and Clinicaltrials.gov. Furthermore, we manually searched the references of relevant articles. The search was not restricted by language or publication status. We included all RCTs of aromatase inhibitors used alone or with other medical therapies for ovulation induction in women of reproductive age with anovulatory PCOS. Two review authors independently selected trials, extracted the data and assessed trial quality. Studies were pooled where appropriate using a fixed effect model to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs) for most outcomes and risk differences (RDs) for ovarian hyperstimulation syndrome (OHSS). The primary outcomes were live birth and OHSS. Secondary outcomes were pregnancy, miscarriage and multiple pregnancy. The quality of the evidence for each comparison was assessed using GRADE methods. We included 26 RCTs (5560 women). In all studies the aromatase inhibitor was letrozole. Live birth (12 RCTs) One RCT compared letrozole with placebo in women who were clomiphene resistant and the results were inconclusive (OR 3.17, 95% CI 0.12 to 83.17, n=36) Nine RCTs compared letrozole with clomiphene citrate (with or without adjuncts) followed by timed intercourse. The birth rate was higher in the letrozole group (OR 1.63, 95% CI 1.31 to 2.03, n=1783, I<sup>2</sup>=3%) Two RCTs compared letrozole with laparoscopic ovarian drilling. There was no apparent difference in pregnancy rates. OHSS was assessed in 15 RCTs (3144 women) OHSS occurred in 38% of women in the placebo group and 14% of women in the letrozole group (RD -0.24, 95% CI -0.44 to 0.01) OHSS is less likely to occur with letrozole. Most RCTs demonstrated a trend towards fewer side effects with letrozole compared to clomiphene. Aromatase inhibitors are as effective as clomiphene citrate for ovulation induction and may be a useful alternative to clomiphene treatment of anovulatory subfertility. More trials are needed to confirm these results.

Language: English

4. Aromatase inhibitors for subfertile women with polycystic ovary syndrome

Citation: The Cochrane database of systematic reviews, 2014, vol./is. 2/(CD010287), 1469-493X (2014)

Author(s): Franki S., Kremer J.A., Nelen W.L., Farquhar C.

Abstract: Background: In women, anti-Mullerian hormone (AMH) is exclusively produced by granulosa cells of ovarian follicles during the early stages of follicle development. After an initial increase until early adulthood, AMH concentrations slowly decrease with increasing age until becoming undetectable ~5 years before menopause when the stock of primordial follicles is exhausted. However, major individual variability exists in the pace of follicle pool depletion and the initial size of the follicle pool, reflected by a wide range of age at menopause. Individual AMH serum concentration does accurately reflect the size of the pool of antral follicles, representing the quantity of the remaining primordial follicles. Accordingly, AMH levels may vary significantly in women of the same chronological age, allowing AMH to predict the remaining length of a woman’s reproductive lifespan. methods: Following 10 years of intense clinical research in this area (with over 300 papers published in core clinical journals every year), the level of evidence justifying use of AMH in ovarian reserve testing is rapidly increasing. We have conducted a summarizing review regarding all evidence published. Results: Many studies have convincingly demonstrated that AMH is the best currently available measure of ovarian reserve under a variety of clinical situations, such as infertility treatment (especially IVF), the forecasting of reproductive lifespan, ovarian dysfunction (especially polycystic ovary syndrome) and gonadotoxic cancer treatment or ovarian surgery. Moreover, AMH may help to individualize dosing for ovarian stimulation thereby improving the efficiency and safety of IVF. However, there are concerns about the performance of the AMH assay under different conditions regarding storage of samples and handling techniques. Therefore an international guideline for laboratories and a reference preparation are needed to make test results between laboratories truly comparable. Conclusions: AMH is the best current available measure of ovarian reserve for different clinical conditions. However, prospective well-powered studies comparing different infertility treatment strategies based on initial AMH levels using appropriate end-points, such as live birth and cost-effectiveness, are urgently awaited. Such studies could represent a true step forward in rendering counseling and infertility care more patient tailored. The Author 2014.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Human reproduction update at Human Reproduction Update

Full text: Available Human reproduction update at No link? Ask Salisbury Healthcare Library - please click here to request article.
evidence of a difference between the groups in live birth rate (OR 1.19, 95% CI 0.76 to 1.86, n=407, I²=0%) OHSS (16 RCTs) There was no evidence of a difference in OHSS rates when letrozole was compared with placebo (one RCT, n=36), clomiphene citrate (with or without adjuncts) followed by timed intercourse (nine RCTs, n=2179), clomiphene citrate (with or without adjuncts) followed by intrauterine insemination (IUI) (two RCTs, n=1494), laparoscopic ovarian drilling (one RCT, n=260) or anastrozole (one RCT, n=220). Events were absent or very rare, and no study had more than 2 cases of OHSS. Clinical pregnancy (25 RCTs) One RCT compared letrozole versus placebo in women who were clomiphene resistant and the results were inconclusive (OR 3.17, 95% CI 0.12 to 83.17, n=36)Fourteen RCTs compared letrozole versus clomiphene citrate (with or without adjuncts) followed by timed intercourse. The pregnancy rate was higher in the letrozole group (OR 1.32, 95% CI 1.09 to 1.60, n=2066, I²=25%)Three RCTs compared letrozole versus clomiphene citrate (with or without adjuncts) followed by IUI. The pregnancy rate was higher in the letrozole group (OR 1.71, 95% CI 1.30 to 2.25, n=1597)Three RCTs compared letrozole versus laparoscopic ovarian drilling. There was no evidence of a difference in the clinical pregnancy rate (OR 1.14, 95% CI 0.80 to 1.65, n=553, I²=0%)Two RCTs compared letrozole versus anastrozole, one RCT compared a five day versus a 10 day administration protocol for letrozole and another RCT compared 5 mg of letrozole versus 7.5 mg of letrozole. There was no evidence of a difference in the clinical pregnancy rate in these comparisons.The quality of the evidence was rated as low for live birth and pregnancy outcomes. The reasons for downgrading the evidence were poor reporting of study methods, possible publication bias and the tendency for studies that reported live birth to report higher clinical pregnancy rates in the letrozole group than studies that failed to report live birth (suggesting that results might be somewhat less favourable to letrozole if all studies reported live birth). Letrozole appears to improve live birth and pregnancy rates in subfertile women with anovulatory PCOS, compared to clomiphene citrate. The quality of this evidence is low and findings should be regarded with some caution. There appears to be no difference in effectiveness between letrozole and laparoscopic ovarian drilling, though there were few relevant studies. OHSS was a very rare event, with no occurrences in most studies.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Wiley at Cochrane Library, The

5. Assisted hatching and intracytoplasmic sperm injection are not associated with improved outcomes in assisted reproduction cycles for diminished ovarian reserve: An analysis of cycles in the United States from 2004 to 2011
Citation: Fertility and Sterility, October 2014, vol./is. 102/4(1041-1047.e1), 0015-0282;1556-5653 (01 Oct 2014)
Author(s): Butts S.F., Owen C., Mainigi M., Senapati S., Seifer D.B., Dokras A.
Language: English
Abstract: Conclusion(s): In initial ART cycles for which the only indication relates to a diagnosis of DOR, AH and ICSI are not associated with improved live birth rates.
Publication type: Journal: Review
Source: EMBASE
Full text: Available FERTILITY AND STERILITY at No link? Ask Salisbury Healthcare Library - please click here to request article.
Full text: Available FERTILITY AND STERILITY at Salisbury District Hospital Healthcare Library

6. Assisted reproduction for postmenopausal women
Citation: Human Fertility, September 2014, vol./is. 17/3(223-230), 1464-7273;1742-8149 (September 2014)
Author(s): Ekberg M.E.
Language: English
Abstract: With increasing longevity, an ageing population and advances in assisted reproductive technologies (ART), a greater number of women are deciding to have a child and become a mother in their later years. With this social and demographic change, an important social and ethical debate has emerged over whether single and/or married postmenopausal women should have access to ARTs. The aim of this paper is to address this question and review critically the arguments that have been advanced to support or oppose the use of ART by older women. The arguments presented consider the consequences for the individual, the family and wider society. They cover the potential physical and emotional harm to the older woman, the possible impact on the welfare and wellbeing of the future child, and the impact on the norms, values, customs and traditions of society. After reviewing the evidence, and weighing the opposing arguments, this paper concludes that there is no moral
justification for a restriction on the use of ART by postmenopausal women. Allowing access to ART for postmenopausal women is an extension of reproductive autonomy and procreative rights in an age where the promotion of agency, autonomy, individual choice and human rights is paramount. 2014 The British Fertility Society.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Human fertility (Cambridge, England)* at No link? Ask Salisbury Healthcare Library - please click here to request article.

7. **Assisted reproductive technology - IVF treatment in Ireland: A study of couples with successful outcomes**  
**Citation:** Human Fertility, September 2014, vol./is. 17/3(165-169), 1464-7273;1742-8149 (September 2014)  
**Author(s):** Mahon E., Cotter N.  
**Language:** English  
**Abstract:** This article describes the experiences of twelve Irish couples who had successful IVF treatment in Ireland. Irish Medical guidelines specify that IVF may only be used when no other treatment is likely to be effective. This article is based on data drawn from a longitudinal research study by Cotter (2009) which tells the stories of 34 couples who sought fertility treatment. Initially, the women assumed that they would become pregnant when they stopped using contraception. As a couple, it was the 'right time' for them to have a child - they were ready, socially and financially. For several months they were patient, hoping it would happen naturally. With envy and some despair they watched as their friends had babies. Infertility came as a shock to most of them. They were reluctant to talk about it to anyone, and over time their anxieties were accompanied by feelings of regret, stigma and social exclusion. They finally sought medical treatment. The latter involved a series of diagnostic treatments, which eventually culminated in IVF which offered them a final chance of having a 'child of their own'. While IVF can be clinically assessed in terms of cycle success rates, their stories showed treatment as a series of discoveries, as an extensive range of diagnostic tests and procedures helped to reveal to them where their problems might lie. They described their treatments as a series of sequential 'hurdles' that they had to overcome, which further strengthened their resolve to try IVF. Much more knowledgeable at that stage, they embraced IVF as a final challenge with single minded dedication while drawing on all their psychological and biological resources to promote a successful outcome. Of the 34 couples who took part in the study, twelve got pregnant. Unfortunately, two children died shortly after birth but eighteen babies survived (see Table I). The findings suggest that health policy should raise awareness of infertility, and advise women to become aware of it-just as in the past, when health policy addressed contraception. Increased public knowledge would reduce the stigma attached to the inability to have a baby. In the Irish case, infertility diagnosis should be reviewed with a view to giving eligible couples earlier access to IVF. 2014 The British Fertility Society.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Human fertility (Cambridge, England)* at No link? Ask Salisbury Healthcare Library - please click here to request article.

8. **Biosimilar recombinant follicle stimulating hormones in infertility treatment**  
**Citation:** Expert Opinion on Biological Therapy, October 2014, vol./is. 14/10(1399-1409), 1471-2598;1744-7682 (01 Oct 2014)  
**Author(s):** Santi D., Simoni M.  
**Language:** English  
**Abstract:** Introduction: Follicle stimulating hormone (FSH) is a glycoprotein hormone essential for reproduction both in females and males and it is physiologically produced by the anterior pituitary gland in several isoforms. This heterogeneity is typical also of FSH-containing compounds, both urinary-derived and recombinant products. These compounds are widely used in assisted reproductive technologies (ART), to induce multifollicular development. Recently, the increased cost pressure on healthcare systems and the patent expiration date of widely used biotechnology-derived, recombinant FSH, prompted the pharmaceutical interest in FSH biosimilars.  
**Areas covered:** In 2014, two FSH biosimilars obtained marketing authorization by the European Medicines Agency. Here, we review the biology of natural, extractive and recombinant FSH, the current state of biosimilar FSH, including the legal framework, and aspects to be considered in biosimilar FSH usage. Literature search methodologies included Medline and PubMed research. Expert opinion: Biosimilar FSH preparations are expected
to be biologically and clinically 'non inferior' to the originator product. However, the impact of FSH biosimilars on cost and outcomes of ART is far from being established, since insufficient information is available to demonstrate the pros and cons in the long-term application.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Expert opinion on biological therapy at No link? Ask Salisbury Healthcare Library - please click here to request article.

Citation: Reproductive BioMedicine Online, October 2014, vol./is. 29/4(404-410), 1472-6483;1472-6491 (01 Oct 2014)
Author(s): Machtinger R., Orvieto R.
Language: English
Abstract: Recent data have raised concerns about the detrimental effect of chronic exposure to environmental chemicals. Some chemicals affect the endocrine system (endocrine disruptors) and have been linked to several diseases, including infertility. One such endocrine disruptor is bisphenol A (BPA), a monomer widely used in the plastic industry, with nearly ubiquitous exposure. In this review, data on the effects of BPA on female fertility are summarized. Specifically, its effect is considered on folliculogenesis, oocyte maturation, embryo quality, and implantation, both in animal and human models. Animal studies have shown that BPA might impair prophase I, follicular growth, and implantation, and may be associated with spindle abnormalities. In humans, while in-vitro studies have suggested an association between BPA exposure and impaired oocyte meiosis, clinical evidence indicate possible adverse effects of BPA exposure on IVF outcomes. As human clinical data are still scarce, larger studies are required to further elucidate the effects of BPA exposure on female fertility.
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. Clinical outcomes following selection of human preimplantation embryos with time-lapse monitoring: A systematic review
Citation: Human Reproduction Update, September 2014, vol./is. 20/5(617-631), 1355-4786;1460-2369 (September 2014)
Author(s): Kaser D.J., Racowsky C.
Language: English
Abstract: Background: Time-lapse monitoring (TLM) has emerged as a novel technology to perform semi-quantitative evaluation of embryo morphology and developmental kinetics in assisted reproduction. While this method has already been introduced into clinical practice in many laboratories, it is unclear whether it adds value to conventional morphology. Most studies only report blastocyst formation as the primary end-point. The aim of this systematic review is to provide a critical evaluation of the available studies that report clinical outcomes following embryo selection with TLM. Methods: A literature search in MEDLINE, Cochrane CENTRALand ISIWeb of Knowledge Science Citation Index was performed to identify studies that assess the clinical utility of kinetic markers for non-invasive selection of human embryos with high implantation potential. Only studies published before 31 December 2013 in the English language that report rates of implantation, clinical pregnancy or live birth were included. Results: Two hundred and fifty-one studies were identified by database search and reference list review; only 13 met eligibility criteria and were included in this analysis. The following morphokinetic parameters were assessed: pronuclear dynamics and morphology (n = 3), duration of first cytokinesis and reappearance of nuclei after cleavage (n = 3), time to various cleavage stages (n = 5), duration of various cleavage stages (n = 6), duration of cleavage cycles and mitotic synchronicity (n = 6), and time to morula, blastocyst and hatching (n = 4). Five studies used combined parameter grading to generate a cumulative score, and two studies retrospectively compared implantation rates following embryo selection by conventional morphology alone or with the addition of a hierarchal time-lapse classification. While several studies suggest higher implantation rates for fast-cleaving embryos and those with a timely duration (i.e. all time points within the defined ranges) of the 2-cell and 3-cell stages, no single morphokinetic parameter has been consistently shown to predict implantation potential. Furthermore, there was considerable disagreement regarding not only which parameters are useful, but also what constitutes normal and abnormal intervals for these measurements. Conclusions: While TLM has the
potential to revolutionize clinical embryology, there are currently no high-quality data to support the clinical use of this technology for selection of human preimplantation embryos. Our recommendations for the adoption of this technique are thus limited by the available literature and the lack of robust prospective studies reporting clinical outcomes. Sparse, often incomplete and largely heterogeneous data suggest that TLM may be able to distinguish between high and low-implantation potential embryos. Only one study demonstrated significantly improved clinical pregnancy rates when embryos were selected by TLM in addition to conventional morphology. Prospective studies are currently underway and hopefully will clarify the role of TLM. As more data become available, it is of the utmost importance that groups using TLM share a common nomenclature for measured time points; herein, we have proposed a standardized system for describing any milestone along the preimplantation developmental timeline. Furthermore, future studies must publish completed datasets in an effort to define patient-specific algorithms with the clinically meaningful end-point of implantation, prior to routine adoption in the assisted reproduction technology laboratory. Until such evidence accumulates, selection of embryos by TLM should remain an experimental strategy subject to institutional review and approval.

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

11. Clinical prediction models to inform individualized decision-making in subfertile couples: A stratified medicine approach  
**Citation:** Human Reproduction, September 2014, vol./is. 29/9(1851-1858), 0268-1161;1460-2350 (September 2014)  
**Author(s):** McLernon D.J., Te Velde E.R., Steyerberg E.W., Mol B.W.J., Bhattacharya S.  
**Language:** English  
**Abstract:** Infertility is defined as failure to conceive after 1 year of unprotected intercourse. This dichotomization into fertile versus infertile, based on lack of conception over 12-month period, is fundamentally flawed. Time to conception is strongly influenced by factors such as female age and whilst a minority of couples have absolute infertility (sterility), many are able to conceive without intervention but may take longer to do so, reflecting the degree of subfertility. This natural variability in time to conception means that subfertility reflects a prognosis rather than a diagnosis. Current clinical prediction models in fertility only provide individualized estimates of the probability of either treatment-independent pregnancy or treatment-dependent pregnancy, but do not take account of both. Together, prognostic factors which are able to predict natural pregnancy and predictive factors of response to treatment would be required to estimate the absolute increase in pregnancy chances with treatment. This stratified medicine approach would be appropriate for facilitating personalized decision-making concerning whether or not to treat subfertile patients. Published models are thus far of little value for decisions regarding when to initiate treatment in patients who undergo a period of, ultimately unsuccessful, expectant management. We submit that a dynamic prediction approach, which estimates the change in subfertility prognosis over the course of follow-up, would be ideally suited to inform when the commencement of treatment would be most beneficial in those undergoing expectant management. Further research needs to be undertaken to identify treatment predictive factors and to identify or create databases to allow these approaches to be explored. In the interim, the most feasible approach is to use a combination of previously published clinical prediction models. 2014 The Author.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Oxford University Press NHS Pilot 2014 (NESLi2) at No link? Ask Salisbury Healthcare Library - please click here to request article.  
**Full text:** Available Oxford University Press NHS Pilot 2014 (NESLi2) at Human Reproduction

12. Current controversies in turner syndrome: Genetic testing, assisted reproduction, and cardiovascular risks  
**Citation:** Journal of Clinical and Translational Endocrinology, September 2014, vol./is. 1/3(61-65), 2214-6237 (September 2014)
Author(s): Ackermann A., Bamba V.
Language: English
Abstract: Patients with Turner syndrome (TS) require close medical follow-up and management for cardiac abnormalities, growth and reproductive issues. This review summarizes current controversies in this condition, including: 1) the optimal genetic testing for Turner syndrome patients, particularly with respect to identification of Y chromosome material that may increase the patient’s risk of gonadoblastoma and dysgerminoma, 2) which patients should be referred for bilateral gonadectomy and the recommended timing of such referral, 3) options for assisted reproduction in these patients and associated risks, 4) the increased risk of mortality associated with pregnancy in this population, and 5) how best to assess and monitor cardiovascular risks. 2014 The Authors. Published by Elsevier Inc. All rights reserved.
Publication type: Journal: Review
Source: EMBASE

13. Endometriosis: an overview of Cochrane Reviews
Citation: The Cochrane database of systematic reviews, 2014, vol./is. 3/(CD009590), 1469-493X (2014)
Author(s): Brown J., Farquhar C.
Language: English
Abstract: This overview reports on interventions for pain relief and for subfertility in pre-menopausal women with clinically diagnosed endometriosis. The objective of this overview was to summarise the management. However, in all cases the quality of the evidence was of low quality. For women with pain and endometriosis, suppression of menstrual cycles with gonadotrophin-releasing hormone (GnRH) analogues, the levonorgestrel-releasing intrauterine system (LNG-IUD) and danazol were beneficial interventions. Laparoscopic treatment of endometriosis and excision of endometriomata were also associated with improvements in pain. The evidence on NSAIDs was inconclusive. There was no evidence of benefit with post-surgical medical treatment. In women with endometriosis undergoing assisted reproduction, three months of treatment with GnRH agonist improved pregnancy rates. Excisional surgery improved spontaneous pregnancy rates in the nine to 12 months after surgery compared to ablative surgery. Laparoscopic surgery improved live birth and pregnancy rates compared to diagnostic laparoscopy alone. There was no evidence that medical treatment improved clinical pregnancy rates. Evidence on harms was scanty, but GnRH analogues, danazol and depot progestagens were associated with higher rates than other interventions.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Wiley at Cochrane Library, The

14. Factors associated with the donation and non-donation of embryos for research: A systematic review
Citation: Human Reproduction Update, September 2014, vol./is. 20/5(641-655), 1355-4786;1460-2369 (September 2014)
Author(s): Samorinha C., Pereira M., Machado H., Figueiredo B., Silva S.
Language: English
Abstract: Background: Systematic knowledge on the factors that influence the decisions of IVF users regarding embryodonation for research is a core need for patient-centred policies and ethics in clinical practice. However, no systematic review has been provided on the motivations of patients who must decide embryo disposition. This paper fills this gap, presenting a systematic review of quantitative and qualitative studies, which synthesizes the current body of knowledge on the factors and reasons associated with IVF patients’ decisions to donate or not to donate embryos for research. Methods: A systematic search of studies indexed in PubMed, ISIWoK and PsycINFO, published before November 2013, was conducted. Only empirical, peer-reviewed, full-length, original studies reporting data on factors and reasons associated with the decision concerning donation or non-donation of embryos for research were included. Eligibility and data extraction were performed by two independent researchers and disagreements were resolved by discussion or a third reviewer, if required. The main quantitative findings were extracted and synthesized and qualitative data were assessed by thematic content analysis. Results: A total of 39 studies met the inclusion criteria and were included in the review. More than half of the studies (n = 21) used a quantitative methodology, and the remaining were qualitative (n = 15) or mixed-methods (n = 3) studies. The studies were derived mainly from European countries (n = 18) and the USA (n = 11). The proportion of IVF users who donated embryos for research varied from 7% in a study in France to 73% in a Swiss study. Those
who donate embryos for research reported feelings of reciprocity towards science and medicine, positive views of research and high levels of trust in the medical system. They described their decision as better than the destruction of embryos and as an opportunity to help others or to improve health and IVF treatments. The perception of risks, the lack of information concerning research projects and the medical system and the conceptualization of embryos in terms of personhood were the most relevant motives for not donating embryos for research. Results relating to the influence of sociodemographic characteristics and reproductive and gynaecological history were mostly inconclusive. Conclusions: Three iterative and dynamic dimensions of the IVF patients' decision to donate or not to donate embryos for research emerged from this review: The hierarchization of the possible options regarding embryo disposition, according to the moral, social and instrumental status attributed to embryos; patients' understanding of expectations and risks of the research on human embryos; and patients' experiences of information exchange and levels of trust in the medical-scientific institutions. The Author 2014. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available *Human reproduction update* at Human Reproduction Update

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

15. **Implementing the ESHRE 'poor responder' criteria in research studies: Methodological implications**

**Citation:** Human Reproduction, September 2014, vol./is. 29/9(1835-1838), 0268-1161;1460-2350 (September 2014)

**Author(s):** Papathanasiou A.

**Language:** English

**Abstract:** The Bologna criteria for defining poor ovarian response (POR) during IVF provide a useful template for new research in this field of assisted conception. However, designing studies around the European Society for Human Reproduction and Embryology POR criteria can be methodologically challenging, as the new definition includes various POR subpopulations with diverse baseline characteristics and unknown clinical prognosis. When designing RCTs, potential result bias may be introduced if women from each subpopulation are not evenly allocated between intervention groups. In the case of small or moderate-size RCTs, a single-sequence randomization method may not ensure balanced allocation between groups. Stratified randomization methods provide an alternative methodological approach. Depending on the chosen methodology, patient characteristics and outcomes within each intervention group may be better reported according to relevant subpopulations. 2014 The Author.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available Oxford University Press NHS Pilot 2014 (NESLi2) at No link? Ask Salisbury Healthcare Library - please click here to request article.

**Full text:** Available Oxford University Press NHS Pilot 2014 (NESLi2) at Human Reproduction

16. **Klinefelter syndrome: genetic aspects, characteristics and reproduction--present and future**

**Citation:** Harefuah, June 2014, vol./is. 153/6(342-345, 366), 0017-7768 (Jun 2014)

**Author(s):** Bar G., Lunenfeld E., Levitas E.

**Language:** Hebrew

**Abstract:** Klinefelter syndrome is one of the most common genetic causes of male infertility and the most common cause of primary testicular failure. Beside the infertility issue, the syndrome causes decreases in bone mass, muscle wasting, decline in cognitive ability and increases the risk of diseases such as diabetes mellitus, cancer and cardiovascular diseases. Most men are diagnosed late when fertility problems arise and some even remain undiagnosed. It is probably emerging because of the significant differences in clinical appearance and low "awareness" among primary doctors. Early diagnosis and hormone replacement therapy can significantly improve the quality of patients lives, reduce late health complications, and may even preserve their fertility for a longer period of time. In the past, men with this syndrome, especially those of the non-mosaic type, were considered as having no chance of becoming biological fathers. However today, with the technological development of IVF and the ICSI (intracytoplasmatic sperm injectioni, together with testicular biopsies and sperm extractions (TESE), it is possible to help over 50% of the men who have this syndrome.
17. Limitations of embryo selection methods

Citation: Seminars in reproductive medicine, March 2014, vol./is. 32/2(127-133), 1526-4564 (Mar 2014)

Author(s): Wong K.M., Repping S., Mastenbroek S.

Language: English

Abstract: In in vitro fertilization (IVF), the selection of embryos for transfer is generally based on the morphology of the available embryos. However, not all embryos with good morphology implant and on average only one in four treatments are successful. This has driven a quest for alternative selection methods. The best known alternative selection method is preimplantation genetic screening (PGS), which has been used for over a decade before it was shown to be inferior to morphological selection. Now, new forms of PGS (performing biopsy at another stage of development and new methods for analysis) are emerging, just like alternative noninvasive embryo selection methods. However, the concept that better selection will lead to improved IVF results is not so certain anymore. Evidence is accumulating that all available embryos in an IVF cycle can be cryopreserved and transferred in subsequent cycles without impairing pregnancy rates or maybe even with an improvement in pregnancy rates. Embryo selection will then no longer be able to improve the live birth rate in IVF; it could even lower the live birth rate. Embryo selection will only be able to improve the time to pregnancy, if embryos with the highest implantation potential are transferred first. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

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

18. Lost in transition: Women experiencing infertility

Citation: Human Fertility, September 2014, vol./is. 17/3(154-158), 1464-7273;1742-8149 (September 2014)

Author(s): Cunningham N.

Language: English

Abstract: This paper illustrates key findings from a qualitative doctoral research project exploring women's experience of infertility. Six women maintained treatment diaries, reflecting on their experiences prior to, during and beyond infertility treatment. The following key themes are identified: hopefulness, adaptation, transitioning and shifting focus. The data suggest that treatment, clinic experience and living a life 'on hold' act as turning points within the individual life course. It is at the intersection between treatment and outcome that difficulties negotiating the expected and anticipated life course become illuminated, revealing limited connectivity and transitioning through and beyond the treatment process. This is a critical focus area and one that sets the scene for effective future adaptation. The data suggest that the accessibility of supportive care moving through and beyond treatment is limited. This paper argues that the infertility clinic is a critical space and place and one where effective supportive care may enable effective transitioning beyond the experience of infertility as an unanticipated life course disruption. 2014 The British Fertility Society.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Human fertility (Cambridge, England) at No link? Ask Salisbury Healthcare Library - please click here to request article.

19. Metabolomic assessment of embryo viability

Citation: Seminars in reproductive medicine, March 2014, vol./is. 32/2(141-152), 1526-4564 (Mar 2014)

Author(s): Uyar A., Seli E.

Language: English

Abstract: Preimplantation embryo metabolism demonstrates distinctive characteristics associated with the developmental potential of embryos. On this basis, metabolite content of culture media was hypothesized to reflect the implantation potential of individual embryos. This hypothesis was tested in consecutive studies reporting a significant association between culture media metabolites and embryo development or clinical pregnancy. The need for a noninvasive, reliable, and rapid embryo assessment strategy promoted metabolomics
studies in vitro fertilization (IVF) in an effort to increase success rates of single embryo transfers. With the advance of analytical techniques and bioinformatics, commercial instruments were developed to predict embryo viability using spectroscopic analysis of surplus culture media. However, despite the initial promising results from proof-of-principal studies, recent randomized controlled trials using commercial instruments failed to show a consistent benefit in improving pregnancy rates when metabolomics is used as an adjunct to morphology. At present, the application of metabolomics technology in clinical IVF laboratory requires the elimination of factors underlying inconsistent findings, when possible, and development of reliable predictive models accounting for all possible sources of bias throughout the embryo selection process. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Seminars in reproductive medicine at No link? Ask Salisbury Healthcare Library - please click here to request article.

20. Monitoring of stimulated cycles in assisted reproduction (IVF and ICSI)

Citation: The Cochrane database of systematic reviews, 2014, vol./is. 8/(CD005289), 1469-493X (2014)

Author(s): Kwan I., Bhattacharya S., Kang A., Woolner A.

Language: English

Abstract: Traditional monitoring of ovarian hyperstimulation during in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) treatment has included transvaginal ultrasonography (TVUS) plus serum estradiol levels to ensure safe practice by reducing the incidence and severity of ovarian hyperstimulation syndrome (OHSS) whilst achieving the good ovarian response needed for assisted reproduction treatment. The need for combined monitoring (using TVUS and serum estradiol) during ovarian stimulation in assisted reproduction is controversial. It has been suggested that combined monitoring is time consuming, expensive and inconvenient for women and that simplification of IVF and ICSI therapy by using TVUS only should be considered. To assess the effect of monitoring controlled ovarian hyperstimulation (COH) in IVF and ICSI cycles in subfertile couples with TVUS only versus TVUS plus serum estradiol concentration, with respect to rates of live birth, pregnancy and OHSS. We searched the Menstrual Disorders and Subfertility Group Specialised Register of controlled trials, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, PsycINFO, the National Research Register, and web-based trial registers such as Current Controlled Trials. The last search was conducted in May 2014. There was no language restriction applied. All references in the identified trials and background papers were checked and authors were contacted to identify relevant published and unpublished data. Only randomised controlled trials that compared monitoring with TVUS only versus TVUS plus serum estradiol concentrations in women undergoing COH for IVF and ICSI treatment were included. Three review authors independently selected the studies, extracted data and assessed risk of bias. They resolved disagreements by discussion with the rest of the authors. Outcomes data were pooled and summary statistics were presented when appropriate. The quality of the evidence was rated using the GRADE methods. With this update, four new studies were identified resulting in a total of six trials including 781 women undergoing monitoring of COH with either TVUS alone or a combination of TVUS and serum estradiol concentration during IVF or ICSI treatment. None of the six studies reported our primary outcome of live birth rate. Pooled data showed no evidence of a difference in clinical pregnancy rate per woman between monitoring with TVUS only and combined monitoring (odds ratio (OR) 1.10; 95% confidence interval (CI) 0.79 to 1.54; four studies; N = 617; I^2 = 5%; low quality evidence). This suggests that compared with women with a 34% chance of clinical pregnancy using monitoring with TVUS plus serum estradiol, the clinical pregnancy rate in women using TVUS only was between 29% and 44%. There was no evidence of a difference between the groups in the reported cases of OHSS (OR 1.03; 95% CI 0.48 to 2.20; six studies; N = 781; I^2 = 0%; low quality evidence), suggesting that compared with women with a 4% chance of OHSS using monitoring with TVUS plus serum estradiol, the OHSS rate in women monitored by TVUS only was between 2% and 8%. There was no evidence of a difference between the groups in the mean number of oocytes retrieved per woman (mean difference (MD) 0.32; 95% CI -0.60 to 1.24; five studies; N = 596; I^2 = 17%; low quality evidence). The evidence was low quality for all comparisons. Limitations included imprecision and potential bias due to unclear randomisation methods, allocation concealment and blinding, as well as differences in treatment protocols. Quality assessment was hampered by the lack of methodological descriptions in several studies. This review update found no evidence from randomised trials to suggest that combined monitoring by TVUS and serum estradiol is more efficacious than monitoring by TVUS alone with regard to clinical pregnancy rates and the incidence of OHSS.
number of oocytes retrieved appeared similar for both monitoring protocols. The data suggest that both these monitoring methods are safe and reliable. However, these results should be interpreted with caution because the overall quality of the evidence was low. Results were compromised by imprecision and poor reporting of study methodology. A combined monitoring protocol including both TVUS and serum estradiol may need to be retained as precautionary good clinical practice and as a confirmatory test in a subset of women to identify those at high risk of OHSS. An economic evaluation of the costs involved with the two methods and the views of the women undergoing cycle monitoring would be welcome.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Wiley at Cochrane Library, The

21. OMICS: Current and future perspectives in reproductive medicine and technology
Citation: Journal of Human Reproductive Sciences, July 2014, vol./is. 7/2(73-92), 0974-1208;1998-4766 (01 Jul 2014)
Author(s): Egea R.R., Puchalt N.G., Escriva M.M., Varghese A.C.
Language: English
Abstract: Many couples present fertility problems at their reproductive age, and although in the last years, the efficiency of assisted reproduction techniques has increased, these are still far from being 100% effective. A key issue in this field is the proper assessment of germ cells, embryos and endometrium quality, in order to determine the actual likelihood to succeed. Currently available analysis is mainly based on morphological features of oocytes, sperm and embryos and although these strategies have improved the results, there is an urgent need of new diagnostic and therapeutic tools. The emergence of the -OMICS technologies (epigenomics, genomics, transcriptomics, proteomics and metabolomics) permitted the improvement on the knowledge in this field, by providing with a huge amount of information regarding the biological processes involved in reproductive success, thereby getting a broader view of complex biological systems with a relatively low cost and effort.

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

22. Post-embryo transfer interventions for assisted reproduction technology cycles
Citation: The Cochrane database of systematic reviews, 2014, vol./is. 8/(CD006567), 1469-493X (2014)
Author(s): Abou-Setta A.M., Peters L.R., D'Angelo A., Sallam H.N., Hart R.J., Al-Inany H.G.
Language: English
Abstract: In women undergoing in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI), embryos transferred into the uterine cavity can be expelled due to many factors including uterine peristalsis and contractions, low site of deposition and negative pressure generated when removing the transfer catheter. Techniques to reduce the risk of embryo loss following embryo transfer (ET) have been described but are not standard in all centres conducting ET. To evaluate the efficacy of interventions used to prevent post-transfer embryo expulsion in women undergoing IVF and ICSI. We searched the Menstrual Disorders and Subfertility Group Specialised Register of controlled trials to June 2014 and PubMed, MEDLINE, EMBASE, CENTRAL, PsycINFO, CINAHL, World Health Organization ICTRP, and trial registers from inception to June 2014, with no language restrictions. Additionally, we handsearched reference lists of relevant articles, and ESHRE and ASRM conference abstracts. We included randomised controlled trials (RCTs) of interventions used to prevent post-transfer embryo expulsion in women undergoing IVF and ICSI. Two review authors independently screened titles and abstracts and reviewed the full-texts of all potentially eligible citations to determine whether they met our inclusion criteria. Disagreements were resolved by consensus. Two review authors independently extracted data and assessed the risk of bias of included trials using standardised, piloted data extraction forms. Data were extracted to allow intention-to-treat analyses. Disagreements were resolved by consensus. The overall quality of the evidence was rated using GRADE methods. We included four RCTs (n = 1392 women) which administered the following interventions: bed rest (two trials), fibrin sealant (one trial), and mechanical closure of the cervix (one trial). Our primary outcome, live birth rate, was not reported in any of the included trials; nor were the data available from the corresponding authors. For the ongoing pregnancy rate, two trials comparing more bed rest with less bed rest
showed no evidence of a difference between groups (odds ratio (OR) 0.88; 95% confidence interval (CI) 0.60 to 1.31, 542 women, I(2) = 0%, low quality evidence). Secondary outcomes were sporadically reported with the exception of the clinical pregnancy rate, which was reported in all of the included trials. There was no evidence of a difference in clinical pregnancy rate between more bed rest and less bed rest (OR 0.88; 95% CI 0.60 to 1.31, 542 women, I(2) = 0%, low quality evidence) or between fibrin sealant and usual care (OR 0.98; 95% CI 0.54 to 1.78, 211 women, very low quality evidence). However, mechanical closure of the cervix was associated with a higher clinical pregnancy rate than usual care (OR 1.92; 95% CI 1.40 to 2.63, very low quality evidence). The quality of the evidence was rated as low or very low for all outcomes. The main limitations were failure to report live births, imprecision and risk of bias. Overall, the risk of bias of the included trials was high. The use of a proper method of randomisation and allocation concealment was fairly well reported, while only one trial clearly reported blinding. There was no evidence that any of the interventions had an effect on adverse event rates but data were too few to reach any conclusions. There is insufficient evidence to support any specific length of time for women to remain recumbent, if at all, following embryo transfer, nor is there sufficient evidence to recommend the use of fibrin sealants added to the embryo transfer fluid. There is very limited evidence to support the use of mechanical pressure to close the cervical canal following embryo transfer. Further well-designed and powered studies are required to determine the true effectiveness and safety of these interventions.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Wiley at Cochrane Library, The

23. Potential pathophysiological mechanisms of the beneficial role of endometrial injury in in vitro fertilization outcome
Citation: Reproductive Sciences, August 2014, vol./is. 21/8(955-965), 1933-7191;1933-7205 (August 2014)
Author(s): Siristatidis C., Vrachnis N., Vogiatzi P., Chrelias C., Retamar A.Q., Bettocchi S., Glujovsky D.
Language: English
Abstract: Successful embryo implantation is a complex process that involves multiple biological mechanisms and reciprocal interactions between the embryo and the proliferated endometrium. In this review, we provide an informative contribution on the pathways underlying the beneficial nature of endometrial injury toward improving implantation rates of embryos conceived and through in vitro fertilization. The evidence published to date are in favor of inducing local endometrial injury in the preceding cycle of ovarian stimulation to improve pregnancy outcomes in women with unexplained and recurrent implantation failure. Endometrial injury triggers a series of biological responses but the findings suggest that no particular pathway is solely adequate to explain the association between trauma and improved pregnancy rates rather than a cluster of events in response to trauma which benefits embryo implantation in ways both known and unknown to the scientific community. The Author(s) 2014.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Reproductive sciences (Thousand Oaks, Calif.) at No link? Ask Salisbury Healthcare Library - please click here to request article.

24. Preimplantation genetic screening: Back to the future
Citation: Human Reproduction, September 2014, vol./is. 29/9(1846-1850), 0268-1161;1460-2350 (September 2014)
Author(s): Mastenbroek S., Repping S.
Language: English
Abstract: All agree that in hindsight the rapid adoption of preimplantation genetic screening (PGS) using cleavage stage biopsy and fluorescence in situ hybridization (FISH) in routine clinical practice without proper evaluation of (cost-)effectiveness basically resulted in couples paying more money for a less effective treatment. Now, almost 20 years later, we are on the verge of a new era of PGS. But have things really changed or are we simply going back to the future? 2014 The Author.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Oxford University Press NHS Pilot 2014 (NESLi2) at No link? Ask Salisbury Healthcare Library - please click here to request article.
25. Recurrent implantation failure: The role of the endometrium

**Citation:** Journal of Reproduction and Infertility, October 2014, vol./is. 15/4(173-183), 2228-5482;2251-676X (01 Oct 2014)

**Author(s):** Timeva T., Shterev A., Kyurkchiev S.

**Language:** English

**Abstract:** The success rate of reproductive treatment methods depends on many different factors. The most important and discussed ones in the literature are maternal age, the causes of infertility, the ovarian response to stimulation, the influence of the male factor and sperm quality, embryo quality and the various uterine pathologies. Some couples fail repeatedly after transferring good quality embryos without any obvious reason and this becomes a major continuing problem after IVF/ICSI procedures. It can be speculated that in these couples, insufficiency of the endometrium might be a possible reason for implantation failure. This review article summarized current literature describing the consecutive endometrial procedures involved in successful embryo implantation. It is believed that efforts to align criteria for definition of recurrent implantation failure (RIF) and attempts to classify different RIF types would develop guidelines for treatment procedures which would result in an increase in patients' opportunities to conceive.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available *Journal of Reproduction & Infertility* at No link? Ask Salisbury Healthcare Library - please click here to request article.

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**Citation:** Fertility & Sterility, August 2014, vol./is. 102/2(460-468.e3), 0015-0282;1556-5653 (2014 Aug)

**Author(s):** Irani M, Merhi Z

**Language:** English

**Abstract:** OBJECTIVE: To report an update on the role of vitamin D (VD) in ovarian physiology with a focus on genes involved in steroidogenesis, follicular development, and ovarian reserve, as well as ovulatory dysfunction associated with polycystic ovary syndrome (PCOS), and ovarian response to assisted reproductive technology (ART). DESIGN: Systematic review. SETTING: Not applicable. PATIENT(S): Human, animal, and cell culture models. INTERVENTION(S): Pubmed literature search. MAIN OUTCOME MEASURE(S): Granulosa cell function, serum antimullerian hormone (AMH), AMH and its receptor gene expression, soluble receptor for advanced glycation end-products (sRAGE), PCOS parameters, and ART outcome. RESULT(S): In human granulosa cells, VD alters AMH signaling, FSH sensitivity, and progesterone production and release, indicating a possible physiologic role for VD in ovarian follicular development and luteinization. In the serum, 25-hydroxyvitamin D (25OH-D) is positively correlated with AMH, and appropriate VD supplementation in VD-depleted women can suppress the seasonal changes that occur in serum AMH. In VD-deficient women with PCOS, VD supplementation lowers the abnormally elevated serum AMH levels, possibly indicating a mechanism by which VD improves folliculogenesis. The antiinflammatory sRAGE serum levels significantly increase in women with PCOS after VD replacement. Although follicular fluid 25OH-D correlates with IVF outcomes, there is a lack of data pertaining to the impact of VD supplementation on pregnancy rates following IVF. CONCLUSION(S): This review underscores the need for understanding the mechanistic actions of VD in ovarian physiology and the critical need for randomized trials to elucidate the impact of VD supplementation on controlled ovarian hyperstimulation/IVF outcome and ovulatory dysfunction associated with PCOS. Copyright 2014 American Society for Reproductive Medicine. Published by Elsevier Inc. All rights reserved.

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

**Source:** MEDLINE

**Full text:** Available FERTILITY AND STERILITY at No link? Ask Salisbury Healthcare Library - please click here to request article.

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

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27. Strategies for fertility preservation in young early breast cancer patients

**Citation:** Breast, October 2014, vol./is. 23/5(503-510), 0960-9776;1532-3080 (01 Oct 2014)

**Author(s):** Tomasi-Cont N., Lamberti M., Hulsbosch S., Peccatori A.F., Amant F.

**Language:** English
Abstract: Diagnosis of breast cancer in young women poses a threat to fertility. Due to a recent trend of delaying pregnancy, an increasing number of breast cancer patients in reproductive age wish to bear children. Health care providers have the responsibility to know how to manage fertility issues in cancer survivors. Oncofertility counseling is of great importance to many young women diagnosed with cancer and should be managed in a multi-disciplinary background. Most of young breast cancer patients are candidate to receive chemotherapy, which could lead to premature ovarian failure. A baseline evaluation of ovarian reserve may help in considering the different fertility preservation options. The choice of the suitable strategy depends also on age, type of chemotherapy, partner status and patients' motivation. Various options are available, some established such as embryo and oocyte cryopreservation, some still experimental such as ovarian tissue cryopreservation and ovarian suppression with GnRHa during chemotherapy. An early referral to a reproductive specialist should be offered to patients at risk of infertility who are interested in fertility preservation.

Publication type: Journal: Review
Source: EMBASE

Full text: Available Breast (Edinburgh, Scotland) at No link? Ask Salisbury Healthcare Library - please click here to request article.

28. Surgical intervention versus expectant management for endometrial polyps in subfertile women

Citation: The Cochrane database of systematic reviews, 2014, vol./is. 8/(CD009592), 1469-493X (2014)

Author(s): Jayaprakasan K., Polanski L., Sahu B., Thornton J.G., Raine-Fenning N.

Language: English

Abstract: Endometrial polyps, which are benign growths of the endometrium, may be a factor in female subfertility. Possible mechanisms include physical interference with gamete transport, alteration of the endometrial milieu and unresponsiveness to the cyclical global endometrial changes. As such polyps remain mostly asymptomatic, their diagnosis is often incidental during routine investigations prior to embarking on assisted reproductive treatment. Transvaginal sonography, hysterosalpingography and saline infusion sonography are the diagnostic tools most commonly employed. However, hysteroscopy remains the gold standard for diagnosis, as well as for treatment. Due to the possible effect of endometrial polyps on fertility, their removal prior to any subfertility treatment is widely practiced. To determine the effectiveness and safety of removal of endometrial polyps in subfertile women. Electronic databases were searched, including the Cochrane Menstrual Disorders and Subfertility Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, PsycINFO, CINAHL and trial registers. The reference lists of identified articles were checked. The last search was performed on 30 July 2014. Only randomised controlled trials, reporting pregnancy or live birth rates and complication rates as primary or secondary outcomes, in which polyps were removed surgically prior to treatment of subfertility were eligible for inclusion. The diagnosis of endometrial polyps was required to be made by transvaginal ultrasound, hysterosalpingography, saline infusion, sono-hysterography or hysteroscopy. Any surgical technique of polyp removal was acceptable, with no intervention in the control groups. Two review authors independently screened the titles, abstracts and full articles to assess their suitability for inclusion in this review. Quality assessment was attempted independently by two authors with discrepancies being settled by consensus or consultation with a third review author. No data extraction was performed due to the absence of useable data in the one eligible study. If there had been data to include, two review authors would have independently extracted the data from the studies using a data extraction form designed and pilot tested by the authors. Any disagreements would have been resolved by discussion or by a third review author. Only one randomised controlled trial of endometrial polypectomy was identified for inclusion. However, a single set of data could not be extracted from this study due to internal inconsistencies of the results reported. Attempts to contact the authors to resolve the issue were unsuccessful, by phone, post and e-mail. Removal of endometrial polyps in subfertile women is commonly being performed in many countries with an aim to improve the reproductive outcome. We did not identify any analysable randomised trials which would allow us to reach any sound scientific conclusions on the efficacy of endometrial polypectomy in subfertile women. Well designed, methodologically sound, randomised controlled trials are urgently needed.

Publication type: Journal: Review
Source: EMBASE

Full text: Available Wiley at Cochrane Library, The

29. Surgical interventions to improve in vitro fertilization outcomes: A systematic review of the literature
Background: Various gynecologic pathologies affect in-vitro fertilization (IVF) treatment detrimentally. Timely management of these pathologies could improve IVF outcomes. However, there is a lack of evidence-based guidelines on the appropriate surgical interventions prior to starting IVF treatment.

Materials and Methods: The current authors systematically reviewed the literature published on surgical interventions described for different gynecologic pathologies related to IVF outcomes and summarized the literature available according to its level of evidence (Scottish Intercollegiate Guidelines Network [SIGN] classification).

Results: This review found that resection of an endometrial polyp diagnosed before the start of an IVF cycle is recommended (level: 1-), whereas management of polyps diagnosed after the start of controlled ovarian stimulation should be individualized (level: 1-). Removal of subserosal uterine fibroids may not be warranted before IVF (level: 1-). There is insufficient evidence regarding the role of myomectomy for managing noncavity distorting intramural fibroids to improve IVF outcomes (level: 1-). Removal of submucosal fibroids is likely to improve IVF outcomes (level: 1-). Data from observational studies suggested that uterine septum resection before IVF treatment may be of benefit, but further evidence from randomized controlled trials is required (level: 2++). Laparoscopic salpingectomy or tubal occlusion improves IVF pregnancy rates in women with hydrosalpinges (level: 1+). There is no evidence to support surgical treatment (aspiration or cystectomy) of ovarian endometrioma over expectant management (level: 1+). Laparoscopic ovarian drilling could be a useful adjunct prior to IVF for women who have previously had IVF treatment cycles that were abandoned because of the risk of ovarian hyperstimulation syndrome (OHSS) or who have had severe OHSS in a previous treatment cycle (level: 1). There is insufficient evidence available to determine if surgical excision of peritoneal endometriosis enhances pregnancy rates in an IVF cycle (level: 2-).

Conclusions: There is good evidence for surgical management of endometrial polyps, submucosal fibroids, and tubal hydrosalpinges to improve IVF outcomes. However, well-designed randomized trials are needed urgently to inform clinical practice better regarding surgical interventions for other gynecologic pathologies found prior to IVF treatment.

30. The Bologna criteria for poor ovarian response: The good, the bad and the way forward

Citation: Human Reproduction, September 2014, vol./is. 29/9(1839-1841), 0268-1161;1460-2350 (September 2014)

Author(s): Venetis C.A.

Abstract: The management of poor ovarian response (POR) remains one of the most significant challenges of in vitro fertilization. Numerous interventions have been proposed, yet few have been shown to be beneficial. The most important problem in evaluating the available evidence has been the lack of a standardized definition of POR. The Bologna criteria for POR have been recently introduced to provide a framework allowing future research in this field to be performed on a relatively homogenous population. However, it has been suggested that the population described by the Bologna criteria might not be sufficiently homogenous and for this reason stratified randomization should be used in relevant randomized controlled trials (RCTs). Stratified randomization, besides its advantages, also has important shortcomings and for this reason it should be used only when there is clear evidence mandating such a design. Currently, there is insufficient data to support such practice in RCTs performed on the population described by the Bologna criteria for POR. Until such evidence becomes available, the scientific community should aim at evaluating interventions for POR according to the Bologna criteria in RCTs of sufficient sample size, with proper allocation concealment and masking. 2014 The Author.
31. The risks and outcome of pregnancy in an advanced maternal age in oocyte donation cycles

**Citation:** Journal of Maternal-Fetal and Neonatal Medicine, November 2014, vol./is. 27/16(1703-1709), 1476-7058;1476-4954 (01 Nov 2014)

**Author(s):** Shufaro Y., Schenker J.G.

**Language:** English

**Abstract:** The maternal age at the first and repeated deliveries constantly rises in developed countries due to current social trends that favor values of personal achievements upon procreation. Assisted reproduction technologies and especially the availability of oocyte donation programs extend the age of fecundity to the fifth and sixth decades of life. The ability to conceive and deliver at such age raises serious medical, moral, social and legal concerns regarding the health and welfare of the mother and child will be presented and discussed here.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available *The journal of maternal-fetal & neonatal medicine* : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians at [No link? Ask Salisbury Healthcare Library - please click here to request article.](No link? Ask Salisbury Healthcare Library - please click here to request article.)

32. Time-lapse imaging of preimplantation embryos

**Citation:** Seminars in reproductive medicine, March 2014, vol./is. 32/2(134-140), 1526-4564 (Mar 2014)

**Author(s):** Conaghan J.

**Language:** English

**Abstract:** Time-lapse imaging of preimplantation embryos is a relatively new and developing technology that may allow embryologists to be more objective in scoring embryos, and allow better selection of embryos for transfer and cryopreservation. The technology is easily assimilated into the in vitro fertilization (IVF) laboratory and is used with any preferred culture medium and culture environment. Embryos are loaded into dedicated culture dishes or trays which allow for individual embryo tracking and in some devices, group culture and individual embryo scoring at the same time. The embryos are imaged at regular intervals without removal from the culture environment, and the images can be viewed individually or stitched together to form a video showing complete development from oocyte to blastocyst. Automated or manual review of time-lapse videos can assist in identifying embryos with normal developmental profiles, and in deselecting embryos for consideration for transfer based on abnormal phenotypes. Time-lapse data are used in conjunction with traditional embryo scoring based on morphology to make embryo selection decisions. Improved embryo selection for transfer could allow for more widespread use of elective single embryo transfer without compromising pregnancy rates after IVF. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available *Seminars in reproductive medicine* at [No link? Ask Salisbury Healthcare Library - please click here to request article.](No link? Ask Salisbury Healthcare Library - please click here to request article.)

33. Ultrasound for monitoring controlled ovarian stimulation: a systematic review and meta-analysis of randomized controlled trials

**Citation:** Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, January 2014, vol./is. 43/1(25-33), 1469-0705 (Jan 2014)

**Author(s):** Martins W.P., Vieira C.V., Teixeira D.M., Barbosa M.A., Dassuncao L.A., Nastri C.O.

**Language:** English

**Abstract:** To evaluate the efficacy and safety of monitoring controlled ovarian stimulation (COS) using ultrasonography. We performed a search in April 2013 for randomized controlled trials (RCTs). Studies that compared different methods for monitoring COS, including ultrasound assessment of follicles (alone or combined with hormonal assessment), in at least one group were considered eligible. The search retrieved 1515 records, six of which were eligible. Five studies were included that compared ultrasonography alone with ultrasonography and hormonal assessment (estradiol and/or progesterone) and one study compared 2D and 3D ultrasound monitoring. None of the included studies reported on live birth. Four of the five studies reported on clinical pregnancy (RR, 0.95; 95% CI, 0.78-1.16; n = 611); the confidence interval (CI) was somewhat wide, but allowed us
to conclude that ultrasonography alone differs little from ultrasonography combined with hormonal assessment. Three studies reported on the number of oocytes retrieved (mean difference (MD), 0.8 oocytes; 95% CI, -0.4 to 2.0; n = 474); the CI was somewhat wide and did not permit us to conclude whether ultrasonography alone is better than or similar to ultrasonography and hormonal assessment for this outcome. All five studies reported on ovarian hyperstimulation syndrome (OR, 1.02; 95% CI, 0.47-2.25; n = 725) and only one study reported on miscarriage (RR, 0.37; 95% CI, 0.07-1.79; n = 45); for these two outcomes, the CI was very wide and did not permit us to conclude whether ultrasonography alone is better, similar or less effective than ultrasonography combined with hormonal assessment. For the study comparing 2D and 3D ultrasound, the reported outcomes were clinical pregnancy (RR, 1.00; 95% CI, 0.58-1.73, n = 72) and the number of oocytes retrieved (MD, -0.4 oocytes; 95% CI, -3.6 to 2.9; n = 72); for both, the CI was very wide and did not permit us to conclude whether use of 3D ultrasound is better, similar or less effective than use of 2D ultrasound. Current evidence suggests that monitoring COS only with ultrasonography is unlikely to substantially alter the chances of achieving a clinical pregnancy and the number of oocytes retrieved is similar to that when monitoring with ultrasonography and hormonal assessment.

For the other outcomes and comparisons, the available data are inconclusive. We believe that more studies evaluating the optimal procedure for monitoring COS are needed.

Publication type: Journal: Review
Source: EMBASE

34. Use of ovary culture techniques in reproductive toxicology
Citation: Reproductive Toxicology, November 2014, vol./is. 49/(117-135), 0890-6238;1873-1708 (November 2014)
Author(s): Stefansdottir A., Fowler P.A., Powles-Glover N., Anderson R.A., Spears N.
Language: English
Abstract: There is increasing evidence to indicate that a substantial number of both man-made and naturally occurring chemicals are disruptive to human and wildlife reproductive health. Currently, reproductive toxicology testing is primarily carried out in vivo, however, in the past 50 years, various culture methods have been developed with the aim of growing ovarian follicles in vitro. These culture systems have become a widely used tool in reproductive biology and toxicology. In this review we describe how reproductive toxicology of the ovary is greatly enhanced by in vitro studies. Experiments using in vitro ovarian cultures to understand or detect damage to the ovary itself and to its specialised structures of the follicles and oocytes, allows for faster screening of potential developmental and/or reproductive toxicants. 2014 The Authors.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Reproductive toxicology (Elmsford, N.Y.) at No link? Ask Salisbury Healthcare Library - please click here to request article.

35. Uterine fibroids: Clinical manifestations and contemporary management
Citation: Reproductive Sciences, September 2014, vol./is. 21/9(1067-1092), 1933-7191;1933-7205 (01 Sep 2014)
Author(s): Doherty L., Mutlu L., Sinclair D., Taylor H.
Language: English
Abstract: Uterine fibroids (leiomyomata) are extremely common lesions that are associated with detrimental effects including infertility and abnormal uterine bleeding. Fibroids cause molecular changes at the level of endometrium. Abnormal regulation of growth factors and cytokines in fibroid cells may contribute to negative endometrial effects. Understanding of fibroid biology has greatly increased over the last decade. Although the current armamentarium of Food and Drug Administration-approved medical therapies is limited, there are medications approved for use in heavy menstrual bleeding that can be used for the medical management of fibroids. Emergence of the role of growth factors in pathophysiology of fibroids has led researchers to develop novel therapeutics. Despite advances in medical therapies, surgical management remains a mainstay of fibroid treatment. Destruction of fibroids by interventional radiological procedures provides other effective treatments. Further experimental studies and clinical trials are required to determine which therapies will provide the greatest benefits to patients with fibroids.
Publication type: Journal: Review
36. Whether sperm deoxyribonucleic acid fragmentation has an effect on pregnancy and miscarriage after in vitro fertilization/intracytoplasmic sperm injection: A systematic review and meta-analysis

Citation: Fertility and Sterility, October 2014, vol./is. 102/4(998-1005.e8), 0015-0028;1556-5653 (01 Oct 2014)
Author(s): Zhao J., Zhang Q., Wang Y., Li Y.
Language: English
Abstract: Main Outcome Measure(s): The outcomes of interest were pregnancy rate and miscarriage rate.
Publication type: Journal: Review
Source: EMBASE
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