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ABSTRACT BOOK

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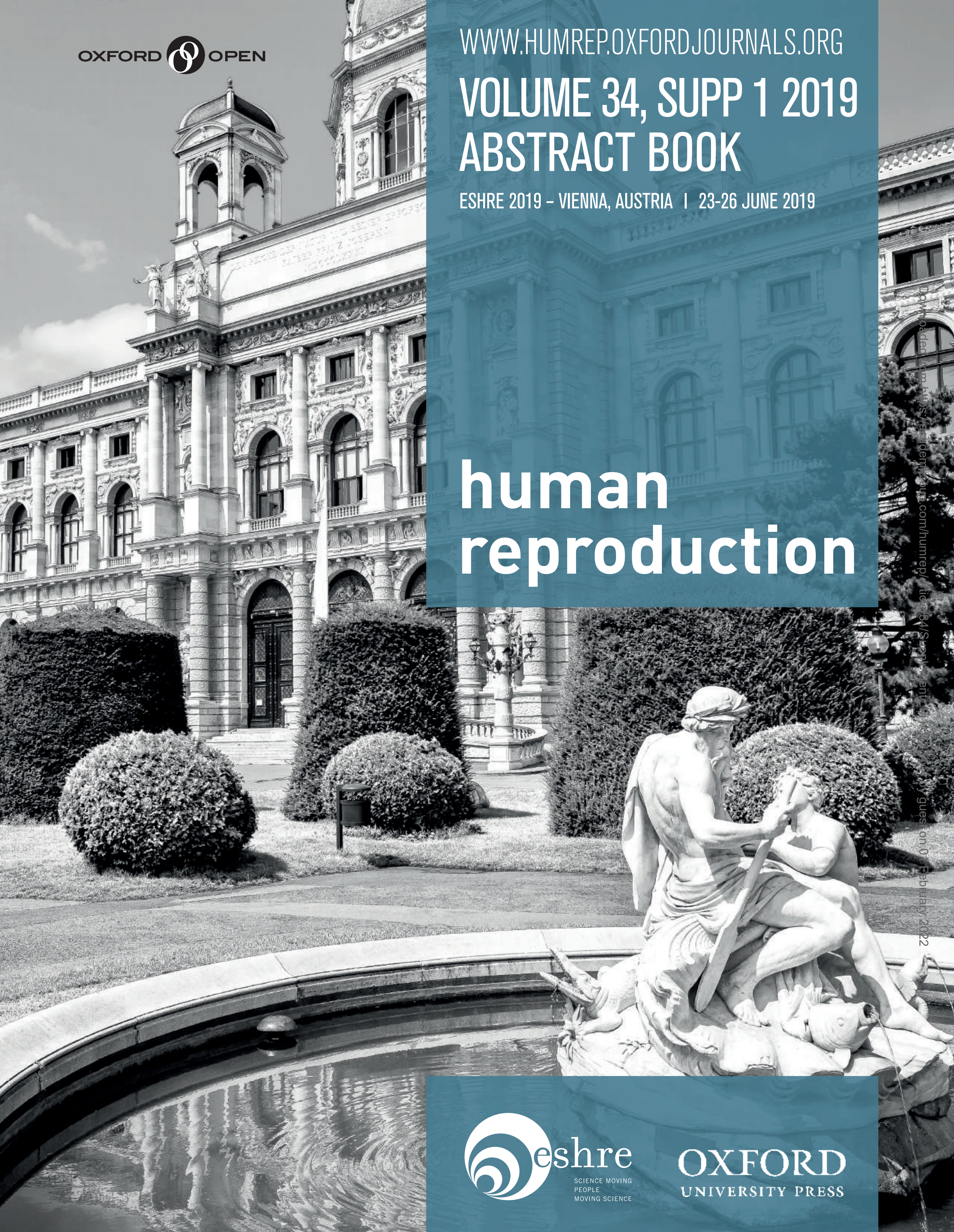
human reproduction



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Abstracts of the 35th Annual Meeting of the European Society of Human Reproduction and Embryology

Vienna

Austria

24 to 26 June 2019

Abstracts

35th Annual Meeting of the
European Society of
Human Reproduction and Embryology,
Vienna, Austria
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human reproduction

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Wider implications of the findings: This is the first study to analyse and question the role of advanced maternal age in explaining the increased risk of poorer birth outcomes amongst children conceived through MAR. This question is of high importance in light of the widespread and increasing use of MAR treatments, especially among older women.
Trial registration number: Not applicable

INVITED SESSION

SESSION 08: OPTIMIZING ART SUCCESS IN POOR PROGNOSIS PATIENTS

Monday 24 June 2019 Haydn 1 11:45–12:45

O-039 Planning IVF treatment in the context of female ageing

O-040 Poor ovarian reserve: Do adjuvant therapies really work?

F.J. Broekmans[1]

[1]*Broekmans- Frank J., Reproductive Medicine, Utrecht, The Netherlands*

Abstract text
Poor ovarian reserve: Do adjuvant therapies really work?

Frank J Broekmans,
Professor Reproductive Medicine and Surgery

Department for Reproductive Medicine

University Medical Center Utrecht

Assisted reproduction technology is applied as a treatment mode for couples with both explained and unexplained infertility. The first step in this treatment is the creation of multiple follicles with the purpose of obtaining the oocytes held within these follicles, creating embryos in the IVF laboratory and replacing the embryos into the uterine cavity. Ovarian stimulation is mostly applied by using exogenous FSH. The response of the ovaries to this exogenous FSH exposure demonstrates a high degree of variation.

From a clinical significance point of view the low ovarian response defined as the yield of less than 5 oocytes is related to an unfavourable prognosis for live birth. The low responder may either have not more than a few antral follicles available or may suffer from a too low FSH exposure to assure the development of all of a normal number of antral follicles present in the ovaries. This leads to a relevant difference between the 'expected' and 'unexpected' low responder, where the latter often has the better prognosis for live birth, although female age will have a crucial additional role here.

Most clinicians try to foresee the low ovarian response category in order to increase the FSH dosage and bring the ovarian response into the normal range (5-15 oocytes), with the expectation that the prospects of pregnancy for the couple will improve. FSH dosage adjustments will most frequently neither alter oocyte number nor improve live birth prognosis in the low responder, especially when the condition is expected, for instance when the AMH or AFC is very low, or in case of female age above 38 years.

Regarding options to enlarge the number of antral follicles by factors that affect the continuous recruitment of follicles from the primordial follicle pool, research has focussed on the paracrine system that regulates this autonomous process. To subtly interfere herein is not easy, and compounds that could alter paracrine settings have sofar failed to show an obvious benefit. Yet many of adjuvant factors researched in fact lean on indirect changes in FSH exposure, thereby negating the relative limited role for FSH in the continuous recruitment.

For drugs like aromatase-inhibitors, oestrogen receptor modulators, androgens, aspirin, LH or growth hormone, effects on oocyte yield in subsequent or concomitant FSH ovarian stimulation have not been consistent or even clearly absent, as are any benefits for prognosis. This may urge for more in-depth research in the feasibility of outside manipulation of this process. Part of this research focusses on 'rejuvenation' of the ovary from its near-depleted state, simply by mechanical tissue disrupture, or by intra-ovarian instillation of paracrine growth factors. All these options are now awaiting rigorous scientific proof of efficacy.

INVITED SESSION

SESSION 09: ESHRE RECOMMENDATIONS FOR GOOD PRACTICE

Monday 24 June 2019 Haydn 3 11:45–12:45

O-041 Recommendations for good practice in ART: The theory

N. Vermeulen[1], **N. Le Clef**[1], **A. D'Angelo**[2], **Z. Veleva**[3], **K. Tilleman**[4]

[1]*ESHRE, Grimbergen, Belgium*
[2]*Cardiff University, College of Biomedical and Life Sciences, Cardiff, United Kingdom*
[3]*Helsinki University and Helsinki University Central Hospital, Department of Obstetrics and Gynecology, Helsinki, Finland*
[4]*Department for Reproductive Medicine, Ghent University Hospital, Ghent, Belgium*

Abstract text
ESHRE has been developing guidelines since 2010, based on a structured evidence-based approach, which is considered the gold standard of medical guidance. Evidence-based guidelines are primarily based on high quality evidence, and are appropriate for areas where such evidence is available for most of the guideline's key questions. Guideline groups can formulate strong and conditional recommendations, depending on the quality of the supporting evidence and other factors including patient perspective, healthcare context and clinicians' expertise. For some topics in the field of Human Reproduction and Embryology, it became clear that an adapted methodology and nomenclature would be appropriate. Therefore, ESHRE has recently developed a manual for the development of (consensus-based) recommendations for good practice. The methodology described is more applicable in areas where there is an opportunity to reduce uncertainty and improve quality of care, but where evidence for most aspects is absent or limited. Topics for recommendations for good practice are different and often more practically oriented than these for evidence-based guidelines. During the presentation, the ESHRE methodology for development of recommendations for good practice, the rationale, and the differences and similarities with evidence-based guidelines, will be discussed. This presentation will be an introduction to the presentation of 2 papers based on the methodology on transvaginal oocyte pick up and ectopic pregnancy.

O-042 Recommendations for good practice in ultrasound - oocyte pick-up: The practice

A. D'Angelo[1], **C. Panayotidis**[2], **N. Amso**[3], **R. Marci**[4], **R. Matorras**[5], **M. Onofriescu**[6], **A. Turp**[7], **F. Vandekerckhove**[8], **Z. Veleva**[9], **N. Vermeulen**[10], **V. Vlaisavljevic**[11]

[1]*University Hospital of Wales- Wales Fertility Institute - Cardiff University-, Wales Fertility Institute, South Glamorgan- Cardiff, United Kingdom*
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[10]*ESHRE, Central office, Brussels, Belgium*
[11]*IVF Adria Consulting, Assisted Reproduction, Maribor, Slovenia*

Abstract text
Study Question: What is good practice in ultrasound, and more specifically during the different stages of transvaginal oocyte retrieval?

Summary Answer: This document provides good practice recommendations covering technical aspects of transvaginal oocyte pick up.
What Is Already Known: Ultrasound guided transvaginal oocyte pick up is a widely performed procedure, but standards for best practice are not available.
Study Design Size, Duration: A working group collaborated on writing recommendations on the practical aspects of transvaginal oocyte pick up.
Participants/Materials, Setting, Methods: This document focused on transvaginal oocyte pick up. Further documents in this series will provide recommendations for other ultrasound procedures in infertility and assisted reproduction.
Main Results And The Role Of Chance: The document presents general recommendations for transvaginal oocyte pick up, and specific recommendations for its different stages, including prior to, during and after the procedure. In addition, information is provided on equipment and materials, possible risks and complications, audit and training.
Limitations Reasons For Caution: The recommendations of this paper were mostly based on clinical expertise as at present only few clinical trials have focused on the oocyte retrieval techniques, and almost all available data are observational. In addition, studies focusing on oocyte pick up were heterogeneous with significant difference in techniques used, which made drafting conclusion and recommendations based on these studies even more challenging.
Wider Implications Of The Findings: These recommendations complement previous guidelines on the management of good laboratory practice in assisted reproduction techniques. Some useful troubleshooting/checklist recommendations were given for easy implementation on clinical practice. These recommendations were aimed to contribute to the standardization of a rather common procedure which is still performed with great heterogeneity.

O-043 Ectopic pregnancy: Classification on imaging

INVITED SESSION
SESSION 10: FERTILITY SOCIETY OF AUSTRALIA EXCHANGE LECTURE
Monday 24 June 2019 Haydn 2 11:45–12:15

O-044 Oocyte-secreted serum biomarkers and reproductive potential in women

A. Riepsamen[1], D.M. Robertson[1,2], R.B. Gilchrist[1], W.L. Ledger[1,3]

[1]*University of New South Wales, Fertility & Research Centre- School of Women's and Children's Health, Sydney, Australia*
[2]*Hudson Institute of Medical Research, Centre for Endocrinology and Metabolism, Clayton Victoria, Australia*
[3]*IVF Australia, Alexandria, Sydney, Australia*

Abstract text
Current serum biomarkers of reproductive potential, such as follicle-stimulating hormone, oestradiol, and anti-Müllerian hormone (AMH), are used to estimate the number of growing follicles in the ovary and to predict the ovarian response to gonadotropin stimulation during assisted reproduction. However, these biomarkers are not derived from the oocyte, and hence only provide an indirect assessment of oocyte function. They provide no information on oocyte quality, which is the rate-limiting factor in female fertility. Bone morphogenetic protein-15 (BMP15) and growth differentiation factor-9 (GDF9) are essentially secreted solely by the oocyte, and are critical for folliculogenesis, oocyte quality and fertility, making these ideal candidates as biomarkers of oocyte function. However, measurement of BMP15 and GDF9 is difficult as serum concentrations of these proteins are expected to be low/undetectable, as these are locally-acting growth factors, and each adult ovary has only ~300,000 oocytes, with the majority of these in a quiescent state. Furthermore, BMP15 and GDF9 exhibit unusual structural variations, including non-covalent dimersation, and there are few molecular tools available to detect these. Currently, there are no validated means to quantitate their concentrations in serum. Our research program aims to develop and validate assays to measure BMP15 and GDF9 in female serum and to investigate their use as biomarkers of female reproductive function. Enzyme-linked immunosorbent assays (ELISAs) for BMP15 and GDF9 were developed in-house and validated for specificity (<0.01% and <0.03%, respectively), sensitivity (24 and 26 pg/ml, respectively) and reproducibility. Recombinant protein standards diluted in parallel with serum samples in dose-response experiments, and serum BMP15 and GDF9 were stable after 3 repeated freeze thaw cycles (1 and 10% reduction in detection, respectively). Validated ELISAs were applied to serum samples from women undergoing infertility treatments (n=154), and from peri- and post-menopausal women (n=28). BMP15 and GDF9 were determined in women relative to age, AMH and number of oocytes retrieved after superovulation for IVF. Serum BMP15 and GDF9 were detectable in 61% and 29% of women, respectively. BMP15 and GDF9 varied 64- and 15-fold, respectively, between women but did not change within an individual during ovarian stimulation with gonadotropins. Furthermore, there was no difference is serum BMP15 or GDF9 between women relative to ovarian stimulation treatment, or between stimulated and unstimulated women. Serum GDF9, but not BMP15, correlated with the number of oocytes retrieved (p=0.058) and was significantly lower in poor responders (p=0.032). Conversely, and where detectable, serum BMP15, but not GDF9, was significantly lower in women over 55 years, compared with women of reproductive age (p=0.018). There was no association between AMH and either of these growth factors. This is the first study to develop and validate assays to quantitate BMP15 and GDF9 in human serum, and to correlate concentrations with female reproductive potential. As oocyte paracrine factors, predictably, BMP15 and GDF9 concentrations were low in serum, in the pg/ml range, several orders of magnitude lower than AMH, making them undetectable in some women with this first-generation assay. Although assay sensitivities require improvement, this study demonstrates the diagnostic potential of oocyte-secreted BMP15 and GDF9 as serum biomarkers in reproductive medicine.

INVITED SESSION
SESSION 11: FERTILIZATION IN THE RESEARCH AND HUMAN IVF LABORATORIES
Monday 24 June 2019 Haydn 4 11:45–12:45

O-045 Breakthroughs in human fertilization

E. Bianchi[1], G. Wright[1]

[1]*Wellcome Sanger Institute, Cell Surface Signalling Laboratory, Hinxton- Cambridge, United Kingdom*

Abstract text
The Molecular basis of sperm-egg recognition
In sexually reproducing species, fertilization represents the first step toward the generation of a new genetically distinct individual. Male and female gametes, which in mammals possess very distinct features, have to recognise and fuse with one another for fertilization to be successful. Spermatozoa are constantly produced in large numbers: they are small motile cells with a densely packed DNA, very scarce cytoplasm and a tail that propels them along the female reproductive tract. The oocytes are rare, with only a few hundred produced over the entire reproductive life of an individual, have a large cytoplasm to support the early embryonic developmental stages, are immotile, and protected by a mesh made of glycoproteins (the Zona Pellucida, ZP). After migrating along the female reproductive tract, the sperm become capable of penetrating the oocyte, the first gamete interaction is the binding of the sperm to the ZP, followed by the passage through the ZP and into the perivitelline space. The last essential step before fusion is the binding of the cell membranes of sperm and egg. Cell fusion finally begins in the equatorial region of the sperm head and guarantees the delivery of the paternal DNA inside the maternal cytoplasm.
It is remarkable that the accurate descriptive knowledge that we have about fertilization does not correspond to a comparable level of understanding of the molecular events. The interactions established by cell surface proteins are