



**Colleen Lynch MSc**  
Training and Scientific Manager

Every year, ESHRE presents a great opportunity to discover the latest research and scientific insights. We hope you enjoy reading our summary of some of the show's most insightful sessions.

### **Genomics and Embryo Testing**

During the ESHRE PGT consortium data reporting session, panel members discussed how it was incorrect to continue to label PGT-A experimental and unproven given data from a number of published RCTs, including ESHRE's own ESTEEM trial, which demonstrated a reduced time to pregnancy and reduced miscarriage rate.

New ESHRE PGT guidelines are currently under review and four papers are due to be published, relating to organization, biopsy, PGT-M and PGT-A/SR. Additionally, Cavagnoli (O-078) presented data demonstrating that blastocyst biopsy is not associated with adverse perinatal or obstetric results in fresh or frozen cycles, and risks are in line with standard IVF cycles.

### **PGT and Morphology and Morphokinetics**

Whether a role remained for morphology or morphokinetics was discussed, with the increasing use of PGT-A for more objective embryo selection. Zaninovic (O-198) implemented a numerical scoring model for 11,365 Day 5 and Day 6 blastocysts and concluded a combination of blastocyst morphology, developmental rate and female age can be used to predict ploidy and implantation in both PGT and standard cycles. In contrast, through the examination of 553 frozen transfers and 4,761 fresh transfer, Tan (O-200) concluded that following PGT-A, morphological differentiators are not meaningful and that Day 5 and Day 6 euploid embryos have similar outcomes.

### **PGT and Mosaic Embryos**

A number of studies were presented, and a summary of current publications, evidencing that mosaic embryos can be transferred and result in successful treatment and healthy live birth.

Rubio (O-103) highlighted recent published guidance from PGDIS and COGEN for the prioritization of embryos for transfer, and last year's paper from Grati et al employing an evidence-based scoring system assigning individual risk for the likelihood of each adverse outcome.

Data presented by Rubio (O-103) and Spinella (O-077) both drew attention to good concordance seen in mosaic embryos with whole chromosome gains or losses, which was reduced where segmental changes are involved. It is agreed that euploid embryos should be prioritized for transfer, but that mosaic embryos should be considered for transfer in their absence. Spinella (O-077) demonstrated embryos with single or double monosomies in <50% cells had a live birth rate equivalent to euploid embryos. However, the summary data presented by Rubio (O-103) did not demonstrate a difference in outcomes between embryos which are mosaic for monosomies and those mosaic for trisomies.

There is consensus that patient counseling with respect to mosaicism is essential pre-treatment, and that follow-up is fundamental. Nizzard (O-104) highlighted that the identification of mosaicism at the embryo stage introduces new challenges in obstetric care and that sharing of information between medical teams is essential. It remains to be seen if these pregnancies, resulting from mosaic embryos, are at higher risk for findings at ultrasound.

### **Non-Invasive PGT-A**

Rubio (O-103) and Madjunkova (O-201) presented promising preliminary data in relation to non-invasive PGT-A and plans for RCTs. This involves the genetic testing of blastocoele fluid or spent culture media.

Rubio (O-103) reported an ongoing implantation rate of 52.9% when the trophectoderm biopsy and spent culture media both gave a euploid result, contrasting with a 16.7% ongoing implantation rate when trophectoderm was euploid but spent culture media was aneuploid. This suggests that the differing results potentially reflect mosaicism.

Madjunkova (O-201) suggested the mechanism of production of cell-free DNA is not apoptosis based on fragment size generated. They were also able to demonstrate that blastocyst morphology doesn't significantly impact DNA yield or concordance rates.

## Endometrial Receptivity

Given the growing popularity of FETs, Vinsonneau (O-021) examined whether the endometrial preparation impacted outcomes. Looking at natural cycles, stimulated cycles (with gonadotrophin) and artificial cycles (with sequential estrogen/progesterone treatment) in a multicenter retrospective study (14,421 cycles), they observed a significant increase in the miscarriage rate and a significant decrease in the live birth rates (LBR) in the artificial cycles compared to the others.

El Hachem (O-024) also examined endometrial preparation, comparing transdermal and vaginal estrogen in artificial cycles. Transdermal estrogen was associated with improved endometrial thickness, shorter treatment duration, and fewer side effects. While clinical outcomes were not impacted, the patient satisfaction was higher in the transdermal group.

Taking a different angle, Entezami (O-128) examined the impact of endometrial preparation on the window of implantation (WOI) in repeated implantation failure (RIF) patients. It was demonstrated that a majority of patients who had suffered from RIF had a delayed WOI, and that acquisition of the receptive phenotype is more gradual, but that using endometrial receptivity to personalise ET day benefited all groups in terms of clinical pregnancy rate (CPR) and LBR.

Beyond endometrial receptivity, some groups have begun examining the microbiota of the endometrium and vagina. Kitaya (O-022) presented preliminary analysis from a prospective case control study (28 RIF patients and 18 control patients), all undergoing IVF treatment. The diversity of the endometrial microbiota was significantly different in the two groups, with pathogen Burkholderia observed within 25% of RIF patients but none of the control patients, suggesting potential involvement.

## Implantation Failure and Miscarriage

Exciting new research at ESHRE included two trials: the PRISM trial (O-047) and TABLET trial (O-048). The former, focusing on progesterone therapy for women suffering a previous miscarriage, and the latter on the increased risk of miscarriage observed in studies examining thyroid antibodies. The PRISM trial showed that incremental improvements in LBR can be achieved in patients with a high order of previous miscarriages, and in patients with threatened miscarriage who have previously experienced one or more, using vaginal micronized progesterone.

The TABLET study data questioned the benefit of routine thyroid function tests as dysfunction does not appear to explain miscarriage. There was only a 9.5% prevalence of thyroid antibodies observed in this study group and no significant difference in the LBR during the trial. Levothyroxine treatment may also have adverse side-effects such as pre-eclampsia and gestational diabetes, but these proved not to be statistically significant. Auto-immune conditions rather than thyroid dysfunction causing pregnancy loss is more likely in women with thyroid antibodies.

Scarpellini (O-126) investigated subcutaneous GM-CSF as a treatment for RIF (O-126). The cytokine promotes leukocyte growth and trophoblast development and the RCT involved 73 patients, 36 of whom received subcutaneous GM-CSF from the day of embryo transfer (single euploid embryo post PGT-A) until the day of  $\beta$ HCG. The pregnancy rate was significantly higher in the group treated with GM-CSF (75% vs 43.2%), possibly linked to improved trophoblast development. GM-CSF can also be employed in supplemented culture media. Kinoshita (P-368) presented data from an RCT investigating the use of GM-CSF media for embryo transfer in FET cycles. Of 473 transfers, 148 used GM-CSF media as opposed to standard one-step media. Transfers using GM-CSF media had a significantly higher CPR and ongoing implantation rate, and a trend towards lower miscarriage rate.

## Sperm

Veltman (O-161) highlighted how male infertility is lagging behind in genetics research and diagnostics and discussed the clear need to develop genomic tests for male infertility. By comparing DNA from patients with azoospermia and severe oligospermia with their unaffected parents, de novo mutations have been identified in the patients, providing target genes for functional studies and further research into male infertility.

Related work in this area is being done by O'Bryan (O-162), using *Drosophila* and mouse models of sperm form and function, linking clinical phenotype to underlying gene and vice versa. Spermatogenesis was discussed in more detail in Session 20 and included presentations highlighting the different gene expression profiles in testicular and ejaculated spermatozoa (O-072) which may develop into RNA-based marker panels to test sperm maturity, the role of retinoic acid in spermatogenesis, suggesting a possible role for vitamin A deficiency in male infertility (O-071), and that as well as predicting the likelihood of sperm retrieval, AZF deletion genotypes can also predict clinical outcome (O-075).