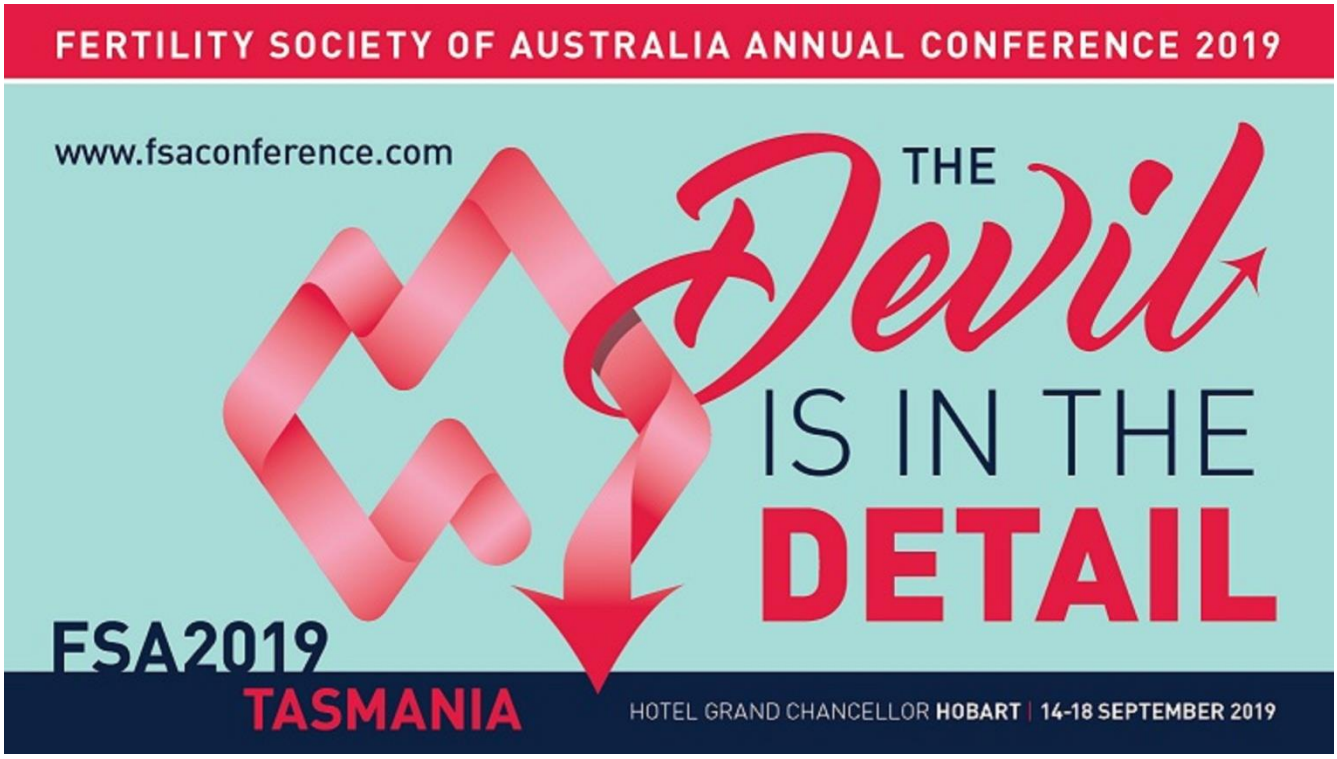

ABSTRACT LISTING

Does the Age of the Sperm Influence Pregnancy Outcome in Assisted Reproduction?

Franca AGRESTA[1], Claire GARRETT[1], Kate STERN[1, 2] and David K GARDNER[1, 3]

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Background:
The concern for older men's sperm has focussed around birth defects, while the impact of paternal age on reproduction, especially using assisted reproductive technologies(ART), has received relatively little attention. This is confirmed by the lack of consensus amongst the key professional bodies about the upper sperm donor age limit, with the HFEA (UK) recommending 41 years (HFEA code of practice: guidance note 11), the ASRM (USA) recommending 40 years (Practice Committee of the American Society for Reproductive Medicine, and Practice Committee of the Society for Assisted Reproductive Technology, 2013), the Human Reproduction Act (Australia) recommending 45 years (Reproductive Technology Accreditation Committee, 2010) and ESHRE (Europe) recommending 50 years (ESHRE task force on ethics and law, 2002). This lack of unanimity demonstrates the paucity of evidence linking increasing male age and reproductive outcomes in ART.

Aim:
To investigate the effect of paternal age on pregnancy outcomes in ART.

Method:
Retrospective analysis of 1289 *in vitro*-fertilisation(IVF) single embryo transfer cycles performed at Melbourne IVF between January 2014 and January 2019 was performed. Effect of paternal age on clinical pregnancy rate was analysed. Only cycles in which the female age was <35years were included; this approach eliminates the negative effects resulting from advanced maternal age and allows for only the variable of paternal age to be investigated. Only women who underwent no more than two controlled ovarian stimulation cycles were included, to control for an etiology that may be attributed to female factor infertility. All cycles were autologous IVF cycles; this assumes the semen parameters were not a confounding variable as could be the case with ICSI cycles. Only single embryo transfers(SET) of fresh or vitrified day 5 embryos were included in the analysis.

Results:
Table 1: Clinical pregnancy rate by paternal ages grouped by <40 years and >40 years.

	Maternal age (yrs)	Paternal age (yrs)	# Clinical Pregnancy Rate (CPR) %
Group 1 (maternal age <35y and paternal age <40y)	<35 (Avg 32)	<40 (Avg 33)	36
Group 2 maternal age <35y and paternal age >40y)	<35 (Avg 33)	>40 (Avg 43)	26#

 # When controlling for female age and normal semen parameters, the clinical pregnancy rate is significantly reduced when the paternal age is >40yrs (p=0.028, Fischer's Exact test)

Conclusions:
Increased paternal age negatively influences the clinical pregnancy rate (p=0.028). In view of the increasing demand for donor sperm, these data suggest that a successful conception may be compromised when older sperm is used and as such an upper age limit for sperm donors may be warranted. For the cases where non-donor sperm is used, these data provide an opportunity to counsel couples and manage their expectations with respect to treatment outcomes which are influenced not only by maternal age, but by also by paternal age.

Is there an Additive Effect of Advanced Maternal Age Combined with Advanced Paternal Age on Outcomes in Assisted Reproduction?

Franca AGRESTA[1], Claire GARRETT[1], Kate STERN[1, 2] and David K GARDNER[1, 3]

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Background:
It has been established that advanced maternal age is linked with reduced fertility.
Further reductions in pregnancy rates are impacted by impaired semen parameters (reduced volume, reduced sperm counts, reduced motility and abnormal morphology) though male factor infertility can be addressed through intracytoplasmic sperm injection. However, the impact of advanced paternal age on pregnancy rates, where semen parameters are normal, has not been well-studied.
As more couples accessing fertility treatment are now mutually of an advanced age, this study endeavours to determine if there is an additive effect of combined maternal and paternal age on pregnancy rates in couples undergoing assisted reproduction.

Aim:
To investigate whether there is an additive effect of advanced maternal age combined with advanced paternal age on pregnancy outcomes in assisted reproduction, despite normal semen parameters.

Method:
Retrospective analysis of 1603 *in vitro*-fertilisation(IVF) single embryo transfer cycles performed at Melbourne IVF between January 2014 and January 2019 was performed. Effect of paternal age on clinical pregnancy rate was analysed. Only cycles in which the female age was >38years were included. Only women who underwent no more than two controlled ovarian stimulation cycles were included, to control for an etiology that may be attributed to female factor infertility. All cycles were autologous IVF cycles; this assumes the semen parameters were not a confounding variable as could be the case with ICSI cycles. Only single embryo transfers(SET) of fresh or vitrified day 5 embryos were included in the analysis.

Results:
Table 1: Clinical pregnancy rate in women with advanced maternal age coupled with paternal ages grouped by <40 years and >40 years.

	Maternal age (yrs)	Paternal age (yrs)	[#] Clinical Pregnancy Rate (CPR) %
Group 1 (maternal age >38y and paternal age <40y)	>38 (Avg 38)	<40 (Avg 35)	29
Group 2 (maternal age >38y and paternal age >40y)	>38 (Avg 40)	>40 (Avg 45)	21[#]

[#] **When coupling advanced maternal age with advanced paternal age, despite normal semen parameters, the clinical pregnancy rate is significantly reduced when the paternal age is >40yrs (p=0.0006, Fischer's Exact test).**

Conclusions:
For women who are of advanced maternal age, where egg quality is compromised, increased paternal age further negatively reduces clinical pregnancy rates, despite normal semen parameters. Sperm from older males may be subject to DNA damage, either from oxidative stress or epigenetic modifications, which do not manifest themselves in the semen parameters, and are likely contributing to the observed reduced pregnancy rates; however this requires further investigation. These data therefore provide an opportunity to counsel couples and manage their expectations with respect to treatment outcomes which are influenced not only by advanced maternal age, but by also by advanced paternal age.

Correlation of Age And Serum Antimullerian Hormone Levels in Predicting Time to Return to Menses in Patients Post Chemotherapy.

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[3] Melbourne IVF, VIC

Background:
Iatrogenic ovarian damage can occur after chemotherapy, radiation and surgery for cancer. There is growing evidence when pretreatment age and AMH (antimullerian hormone) are combined the accuracy of prediction of fall in AMH after treatment, reversibility of ovarian damage and the risk of premature ovarian insufficiency increases.

Aim:
To assess the correlation between pretreatment serum AMH levels, age and time to return to menses after chemotherapy in cancer patients.

Method:
Retrospective data was collected on patients presenting to a major tertiary centre fertility preservation service between the period 2012-2018 with a new diagnosis of cancer who were subsequently facing chemotherapy treatment.

Results:
100 charts were reviewed. Majority of cancers were breast and haematological malignancies. There was a trend towards reduced duration until return of menses for younger women. The preliminary data on baseline AMH and time to return to menses was inconclusive.

Conclusion:
Younger age at the time of chemotherapy treatment may be associated with a faster return to menses.

Cellular Bases of Sperm and Oocyte Ageing

John AITKEN[1]

University of Newcastle and Hunter Medical Research Institute, NSW, Australia,

Background:
The pattern of ageing in male and female gametes is very different. Spermatozoa are stored for a matter of days to weeks in the epididymis and remain capable of fertilization for at least 5 days post ejaculation. On the other hand, oocytes are normally stored for decades in the ovarian cortex and yet only survive for a matter of hours post ovulation, unless they are immortalized by fertilization.

Aim:
To determine the molecular basis of ageing in spermatozoa and oocytes

Method:
Analysis of the biochemical mechanisms responsible for cell senescence in the male and female germ line.

Results:
Ejaculated spermatozoa will remain viable and functional as long as PI3kinase and AKT are phosphorylated. Growth factors such as prolactin and insulin promote survival by maintaining PI3 kinase in an activate, phosphorylated state. Once dephosphorylation of this kinase occurs a truncated apoptotic pathway is activated characterized by mitochondrial ROS formation, lipid peroxidation and DNA damage. Lipid aldehydes generated as a consequence of oxidative stress form adducts with proteins in the mitochondrial electron transport chain leading to electron leakage and yet more ROS generation in a self-perpetuating cycle that culminates in cell death. The fundamental features of senescence in oocytes appears to be very similar. Senescence in these cells is also associated with the induction of oxidative stress associated with mitochondrial ROS generation, lipid peroxidation and formation of protein adducts that compromise oocyte function.

Conclusion:
Senescence in sperm and oocytes is highly correlated with lipid peroxidation and the formation of protein adducts.

Trophectoderm Quality, Cell Survival and Re-Expansion Rates are Predictive of Fetal Heart Potential of Vitrified Blastocysts

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[1] *Melbourne IVF, Melbourne, Australia*

Background:
Blastoccoel re-expansion post blastocyst warming is one predictor shown to correlate to implantation potential. Debate on which parameters that have the highest prognostic value is still inconclusive (Okimura et al., 2009, Lin et al. 2017).

Aim:
The aim of this study was to predict implantation potential for vitrified blastocysts by assessing blastocoel re-expansion, trophectoderm and survival rates post-warming.

Method:
Vitrified blastocysts were scored Good, Fair or Poor for trophectoderm. Vitrified blastocysts (n=621) were warmed for a single frozen embryo transfer (FET) and blastocoel size assessed prior to FET. Blastocoel re-expansion was categorised into full re-expansion (A), ≥50%(B), <50%(C) or collapsed cavity (D). Re-expansion outcomes in conjunction with other parameters including age, embryo development, quality, ploidy status, and cell survival post-warm were correlated to implantation and fetal heart rate.

Results:
Re-expansion was assessed between 0.2-7.7h, and of re-expanded blastocysts, 97.6% re-expanded ≤2h post-warm. Blastocysts re-expanded prior to FET significantly correlates to a higher fetal heart rate of 50.3% vs 12.7% ($p<0.0001$). Only three collapsed blastocysts at FET ≥2h post-warm resulted in a fetal heart (n=48), of which all had high cell survival (≥80%) and good-fair trophectoderm. It was found that increased cell survival post-warm was correlated to a higher fetal heart rate ($p<0.01$). Fetal heart rate was three-fold higher (59.7% vs. 20.0%, $p<0.01$) when blastocysts had good trophectoderm, full re-expansion and ≥80% cell survival compared to blastocysts with poor-fair trophectoderm, collapsed before ET and lower cell survival. There was 0% implantation for collapsed blastocysts that had either poor trophectoderm or had <80% cell survival.

Conclusion:
This study demonstrates the relationship between blastocoel re-expansion, trophectoderm and cell survival post-warm. Observational checks for re-expansion should be conducted 2h post-warm to identify blastocysts with high implantation potential and those that are unsuitable for transfer. This data may be of value in deciding to warm another embryo.

The Presence of Immature GV-Stage Oocytes is a Marker of Poor Oocyte Quality that Predicts Poorer IVF Outcomes: A Pilot Study

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Background:
Female age is known to affect oocyte developmental competence (or quality). DNA damage is another marker of oocyte quality that induces maturation arrest at the germinal vesicle (GV)-stage.

Aim:
To determine whether the presence of GV-oocytes during IVF/ICSI reflects poor oocyte quality.

Methods:
We undertook a prospective cohort study involving 60 IVF/ICSI patients between February 2017 and July 2018 for whom, complete pregnancy outcome data were available.
Patients with GVs at egg pick-up (GV+ group; n=29) were compared to patients without GVs (GV- group; n=31). GV-oocytes from 17 GV+ patients were immunostained for the DNA damage marker, gamma-H2AX, and levels were quantified using confocal microscopy.

Results:
GV+ and GV- patients were similarly aged (35.4 vs. 36.4 years; *P*=0.45) and had comparable yields of mature oocytes (11±6.88 vs. 8.26±4.84; *P*=0.08). Compared with GV- patients, GV+ patients had markedly lower implantation rates (11.8% vs. 30.2%; *P*=0.02) and oocyte utilisation rates (clinical pregnancies and live-births divided by number of mature oocytes) for clinical pregnancy (2.3% vs. 6.8%; *P* = 0.02) and live-birth (1.9% vs. 5.7%; *P*=0.03). Oocyte DNA damage levels were uniformly high regardless of age (*P*=0.61). Thus, GV+ patients exhibit clinical and molecular features of poor oocyte quality that are age-independent; that is, the ageing effect is blunted in these patients due to an inherent predisposition to poor oocyte quality.

Conclusion:
This is the first Australian study of DNA damage in human GV oocytes and its relationship to IVF outcomes. Our findings suggest that GV-oocytes may signal a cohort of oocytes that are of inferior quality. Some patients may be prone to DNA damage with ovarian stimulation; such damage causes some oocytes to remain GV-arrested whilst the others that complete maturation exhibit poor competence. The occurrence of GV-oocytes at egg pickup may therefore influence the decision regarding how many embryos to transfer.

Experiences of Women with PCOS Post Diagnosis, Across the Lifecourse: A Qualitative Investigation

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Background:
Little is known about the health of older women with Polycystic Ovary Syndrome (PCOS). Evidence suggests relatively early onset of diabetes and other cardiometabolic disorders[1]. These women perceive poor health[2] and lifestyle behaviours are less healthy[3], possibly contributing to age-related deterioration[4]. Among young women, poor mental health has consistently been documented[5] but it is unclear whether problems prevail with age.

Aim:
To interview women with PCOS, to understand diagnostic pathways, the extent of physical, mental and emotional health problems, and whether PCOS affects women differently according to their profile of symptoms as they age.

Method:
A narrative approach examined in-depth interviews with women aged ≥35 years, with PCOS, understanding their diagnostic experiences, health and psychosocial outcomes, and profile of symptoms as they age.

Results:
We interviewed 12 women aged 35-49. Average age of diagnosis was 25.3 (range 18-40). Average years since diagnosis was 16.6 years. Most women were diagnosed through problems getting pregnant. Women were very concerned how PCOS was affecting them into later life, a number of them had already been diagnosed with cardiometabolic conditions and the majority had depression. Over half the women were obese, or worked hard with diet and exercise to maintain a reasonable healthy weight, being aware about the impacts of obesity. They were concerned about their daughters, encouraging healthy habits in preparation for a PCOS diagnosis.

Conclusion:
PCOS places a burden on health and impacts quality of life. However, perimenopause and menopause are not considered in PCOS management. Further research understanding the symptoms of PCOS at these life stages is urgently needed.

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Development Rate of Human Blastocysts Before Vitrification is a Significant Predictor of Outcome After Warming and Transfer on Day 5 of a Programmed Cycle: A Retrospective Analysis of Embryo-Specific Criteria in 2311 Single Embryo Transfer Cycles.

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Background:
Morphology and development rate are widely applied embryo grading criteria in use by embryologists to assist in selecting embryos for transfer. Outcomes from the transfer of blastocysts on Day 6 have been shown to be poorer than those on Day 5 (Poulsen et al 2017, Hum Reprod, 32(6), 1238-1243.). There is still disagreement as to whether the outcome of Day 6 blastocysts could be improved by cryopreservation and subsequent transfer on Day 5 of a programmed cycle (Ferreux et al., 2018, Hum Reprod, 33(3), 390-398; Kaye et al., 2017, J Assist Reprod Genet, 34(7), 913-919).

Aim:
The aim of this study was to determine if the outcome of Day 5/6 vitrified/warmed blastocysts were similar when transferred during a programmed cycle.

Method:
Birth outcome data from 2311 SET cycles of vitrified/warmed Day 5/6 blastocysts during an 8-year period (2008 to 2015) were analysed. Transfers were undertaken on the equivalent of Day5 in monitored natural cycles supplemented with exogenous ovulatory trigger, low dose stimulation cycles or cycles with exogenous hormone replacement. Genetically tested, imported, and embryos derived from donor oocytes were excluded from an analysis that used a logistic regression model.

Results:
Day 5 vitrified/warmed blastocysts had a significantly greater survival (88.9% vs 85%; $p<0.0102$) and live birth rate (30.7% vs 19.3%; $p<0.0001$) when compared to Day 6 blastocysts. Controlling for blastocyst grade and expansion level, Day 5 blastocysts had an 80% greater chance of continuing to a live baby than Day 6 blastocysts (OR: 1.80; 95% CI; 1.37-2.35).

Conclusion:
The growth rate of embryos prior to vitrification affects the implantation potential after vitrification which is not corrected by normalizing the day of transfer. Day 6 vitrified/warmed blastocysts have a significantly reduced live birth rate compared to Day 5 blastocysts despite both embryo stages being transferred on Day 5 of a subsequent programmed cycle.

Cellular Details of Effective Blastocyst Vitrification and Warming and Their Effect on Clinical Outcomes.

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Abstract:
The current theory of cell specification during the morula to very early blastocyst stage is that the positional relationship between cells controls differentiation and the subsequent formation of the inner cell mass (ICM), trophectoderm (TE) and blastocoel. Blastocyst vitrification protocols are unique in having to manage these different cell types with differing cell permeability coefficients and large volume shifts across the trophectoderm into and out of the blastocoel. There is still considerable variation in the protocols used for human blastocyst vitrification, warming and survival assessment. Reduced volume vitrification devices with increased cooling and warming rates in addition to vitrification and warming media are now readily available. These rates allow flexibility in the balance between concentrations of cryoprotectants with cell lysis due to ice crystal nucleation and growth during warming. Blastocoel reduction by breaching the junctions between TE cells is used in some IVF units to assist the removal of extracellular water during equilibration and vitrification but there is conflicting evidence as to whether this is necessary. Assisted hatching prior to the transfer of vitrified/warmed blastocyst transfer is also an add on regularly used with questionable efficacy. Embryo specific factors such as blastocyst stage, development rate and morphology grade are important criteria to use for selection of embryos prior to utilization for transfer or vitrification. Recovery rate of the blastocyst and assessment of cell degeneration after vitrification and warming are also important diagnostic criteria. It is essential enough time is made available to assess the warmed blastocyst for these criteria prior to selecting for single embryo transfer (SET).

Evolution and Revolution: Communicating Online in Health!

Hannah BROWN[1]

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Background:
We live in a digital world, where we have seen a shift towards information gathering and data collection online. Now, more than ever, we need to understand the online behavior of those seeking information in health, and in particular, fertility, to make sure we are delivering accessible information, in the right place, at the right time to support decision making and education.

Are we evolving quickly enough, or do we need a complete revolution to communicate with patients, colleagues and peers in the digital age? And how do we demonstrate we are listening when online platforms are designed for speaking?

Come along to learn about the most advanced digital strategies being used to communicate with health globally, and how online communities grow and thrive.

ANZARD 3.0

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Abstract:
The Australian and New Zealand Assisted Reproductive Technology Database (ANZARD) collects treatment and outcome data for all ART and donor insemination treatments performed in Australian and New Zealand clinics. ANZARD is managed by the National Perinatal Epidemiology and Statistics Unit (NPESU) of the UNSW Sydney, and is considered one of the most comprehensive ART registries in the world.
Planned advancements in ANZARD will be presented, including a new ANZARD Data Submission Portal for clinics, and proposed new ANZARD data items. Highlights from the ANZARD 2015 Report will be presented along with more interactive reporting options.

Universal Warming Media – Clinical application

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Background:
Human oocytes and embryos are cryopreserved using one of two methods, slow freezing or vitrification. For a number of years, vitrification has been the favored method worldwide however many slow frozen oocytes and embryos remain in storage. Additionally, within vitrification alone, many different kits and protocols are available on the market. Therefore clinics may receive oocytes or embryos cryopreserved by a number of different methods and sourcing appropriate thawing or warming solutions becomes a very expensive exercise. Therefore the development of "universal" warming media is both a desirable and practical solution. Presented here is our clinical experience of the situation in which the unavailability of a particular warming media prompted the exploration of the implementation of universal warming media for vitrified embryos.

Aim:
To evaluate the implementation of a universal warming media in a clinical setting

Method:
The initial cohort consisted of 16 blastocyst staged embryos consented to procedural training prior to disposal. All 16 embryos were vitrified using Sydney IVF Blastocyst Vitrification Kit and warmed in Vitrolife RapidWarm Omni media. The primary endpoint was morphological assessment of survival at 2 hours post warm. The clinical cohort consisted of 75 blastocyst staged embryos vitrified in Sydney IVF media. These were warmed with Vitrolife RapidWarm Omni media and transferred in a clinical frozen embryo cycle. The primary endpoints were morphological assessment of survival at 2 hours post warm and clinical pregnancy rate.

Results:
The survival rate of the initial 16 embryos at 2 hours post warm was 70%. The survival rate of the 75 embryos transferred in clinical cycles was 96% at 2 hours post warm. The clinical pregnancy rate in this group was 32%.

Conclusion:
Preliminary data suggests warming of vitrified blastocyst embryos in universal media can achieve acceptable survival and clinical pregnancy rates, although a controlled trial is warranted to establish non-inferiority.

Artificial Intelligence in IVF Labs

Simon COOKE[1]

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Talk Overview:
For two decades, almost all clinics in the world have used a variation of the original Gardner alpha-numeric blastocyst grading methodology[1], to try and determine which blastocyst should be ranked higher than the rest of the cohort, and be selected for embryo transfer.

Some manufacturers have tried to improve on this with inbuilt annotated algorithms[2], with other independent authors demonstrating their own *in-house* algorithms have limited use[3]. The time taken for lab staff to perform these annotation processes (particularly in large labs), whilst reducing the intra-observer errors during annotation is a major drawback, and has fueled the desire for full automation.

As systems move away from using 2D static images, and into 3D and 4D decision making, and with the advent of timelapse incubators with operating software that captures huge amounts of data, the next challenge is "how to manage and analyse" these mountains of new data. This has pushed researchers into the area of complex mathematics and computer modelling, and into the world of Artificial Intelligence (AI) to build accurate models that are independent of labs, countries, patient age and culture medium used.

Indeed, the world's first automated timelapse AI analysis system that can accurately predict the fetal heart potential in a cohort of blastocysts with an AUC of 0.93 has recently been published[4].
Deep learning has also been used in other systems, which mostly revolve around the ability for AI to differentiate between embryos of differing morphology[5].

Laboratory methods, and most importantly the usage and degree of automation of AI will be discussed, and the differences explained, and compared to published accuracies.

An exciting new era of embryo assessment based on pure mathematics and proof has already begun.

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Undergoing Multiple Rounds of in Vitro Fertilisation: A Qualitative Interview Study of Women and Couples' Experiences and Decision-making

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[2] *Genea Fertility Clinic, Sydney Australia*
[3] *Family Planning NSW, Sydney, Australia*

Background:
Infertility affects about one in six Australian couples of reproductive age. Regarding In Vitro Fertilisation (IVF) some couples with a good prognosis drop out of treatment prematurely, whilst others continue for multiple cycles, despite limited chance of success. Little is known about what factors contribute to the decision to continue IVF after multiple failed rounds.

Aim:
To explore the psychological factors that contribute to IVF decision-making, and its impact on psychological wellbeing.

Method:
Clinicians and nurses at an Australian private fertility clinic recruited women and couples who had undergone three or more unsuccessful cycles of IVF. Semi-structured face-to-face and telephone interviews were conducted with 20 participants. Interviews were audio-recorded, transcribed and analysed thematically.

Results:
The majority of participants (n=14/20) had decided to or were leaning towards continuing. Participants expressed a range of common factors important in their decision-making about continuing IVF, however decisions were also highly individualised. Most participants expressed they would continue as long as there was any chance of clinical success and no medical reason to stop. For the majority, doctor's advice, and trust in their guidance, were key factors informing their decision. Other factors included participants' perception of success rates, previous cycle outcomes, anecdotal stories of success after multiple rounds, feeling the need to hold onto hope and fear of giving up. The financial impact only seemed to be reported as important for those deciding to stop.

Discussion:
Given the important role of the doctor's guidance in the decision, and that participants often overestimated their chances of success, it is vital fertility specialists give accurate, upfront and transparent information regarding patients' likelihood of success, and continue to communicate this throughout the IVF journey. Anecdotal stories of success against the odds appeared to be influential in the decision to continue and underpinned unrealistic perceptions of possible success.

The Benefits and Harms of Receiving a Polycystic Ovary Syndrome Diagnosis: A Qualitative Study of Women's Experiences

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[3] *University of Pennsylvania, Philadelphia, USA*
[4] *Monash University, VIC, Australia*

Background:
Diagnostic criteria for polycystic ovary syndrome (PCOS) have expanded over time, increasing prevalence and including women with milder phenotypes, despite unclear evidence of benefits and limited investigation of potential harms.

Aim:
To explore the benefits and harms of receiving a PCOS diagnosis in a community sample of women, and investigate how the diagnosis affected their psychosocial wellbeing, lifestyle and behaviour.

Method:
26 women in the Australian community self-reporting a diagnosis of PCOS (reporting mild to severe symptoms) and aged between18-45 years were recruited through Facebook. Women participated in semi-structured interviews, conducted face-to-face or by telephone. Data was analysed thematically using Framework analysis.

Results:
The study identified a range of both positive and negative effects of a diagnosis in the immediate, short and long-term, which were influenced by symptom severity, expectations and experience. For women with previously unexplained and bothersome symptoms, it was a relief to receive a diagnosis, and this resulted in increased understanding about the importance of a healthy lifestyle. By contrast, women with milder symptoms often reported feeling shocked and overwhelmed, experiencing anxiety about the associated long-term risks. Most women experienced prolonged worry and anxiety about infertility, resulting for some in risk taking with contraception, unintended pregnancies, pressure to conceive early or altered life-plans. With time, many women developed positive coping strategies and perceived the diagnosis as valuable, including those who felt they had experienced minimal benefit or even harm.

Conclusion:
Fear of infertility was salient for many women, underscoring the need for accurate information and reassurance of fertility potential. Given the risk of significant consequences, health professionals should use a tailored approach to PCOS diagnosis to increase the benefits that come with appropriate and timely diagnosis for women affected by significant symptoms, while reducing the harms of unnecessarily labelling healthy women for whom benefits are small.

A Systematic Review and Meta-Synthesis of Mobile Device Fertility Applications: More than a Glitch in the Matrix

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[1]*Eve Health, Fertility, Spring Hill, Australia.*

Study question:
The aim of this meta-synthesis was to determine the utility and validity of current mobile device fertility applications and the medical advice given in these applications.

Summary answer:
Despite a significant increase in the number of fertility applications, apps have limited validity, make unrealistic claims of efficacy, and have no established review cycle

What is known already:
Fertility and cycle tracking applications are consistently among the most popular applications on both Android and iOS platforms. Up to 70% of women initiating fertility treatment track their cycles. There is limited published information on how applications are featured or promoted in either store. Furthermore, little systematic assessment has been performed on the validity of the advice offered despite frequent claims of efficacy. Despite data supporting the belief of health professionals that patient apps promote autonomy and and understanding of health, primary healthcare providers have limited familiarity with these applications, and the features frequently used by patients.

Study design, size, duration:
The research protocol followed the published methodology for Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). The research protocol was developed through a staged, iterative process prospectively registered through (PROSPERO ID: 124109). The literature search was conducted of online databases, with a predefined search strategy. All applications up to and including January 8th 2019 were included. Additional applications were identified through snowballing and manual searches of published reviews.

Participants/materials, setting, methods:
iTunes and Google Play were systematically searched for iOs and Android applications, respectively. The analysis included paid and free applications, unrestricted by age but limited to English. Each application was reviewed and scored independently by each researcher based on a predetermined matrix. Descriptors were sorted and categorized in EndnoteX7 (Thomson Reuters). Data analysis and synthesis was performed by computer-assisted qualitative data analysis (NVIVO12, QSR International) and analytic induction in a staged independent framework approach.

Main results and the role of chance:
399 applications were identified in the initial search strategy. 381 applications were included after review of the descriptors. 9 non-English applications and 41 duplicates were removed from the final analysis. 332 applications were included in the systematic review. Between January 2015 and January 2019 there has been a 47% increase in the number of mobile fertility applications (from 225-332). Commonly included features are: conception and contraception tracking, health education, flow and ovulation symptom tracking, cycle length information and prediction. Less then 10% of applications cited published literature or professional guidelines. A significant number of applications made unrealistic and unsubstantiated claims with respect to efficacy.

Limitations, reasons for caution:
Application sources are unreliable, incomplete and subject to commercial imperatives. There is limited transparency in app development, functionality, ownership, and store ranking. This study did not assess user

experience and reproductive outcomes.

Wider implications of the findings:
End users, patients and healthcare professionals, are at risk of accepting the advice and information provided by these applications unchallenged.

Details of luteal phase; when and how?

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Abstract:
Luteal phase support is a crucial part of the IVF treatment, which sometimes have been neglected and treated the same way it was done from decades. While many other aspects of the IVF practice (as ovarian stimulation and laboratory techniques) have evolved and huge effort have been applied to develop them, very few strategies have been described to control and individualize the luteal phase treatment.
Besides nowadays a great number of embryos are transferred in artificial cycles using hormonal therapy. The reasons could be many as identification of OHSS risk, increase of PGT, popularity of the freeze all protocols. Precisely those cycles need a special concern about luteal phase support as there is no natural source of progesterone.
Our group have developed studies which assays the serum progesterone levels at the day of the embryo transfer and compared the results trying to understand the optimal range to enhance embryo implantation and reduce early miscarriage risk. Besides strategies have been developed in order to optimize the progesterone levels of those patients which are out of the ideal range.
The data suggests that luteal phase support may be individualized in order to optimize pregnancy results.

Reproductive Genetic Carrier Screening - The Past, Present and Future

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Abstract:
Carrier screening for genetic conditions has been possible since the 1970s. Screening for Tay-Sachs disease and haemoglobinopathies was possible because for each, there is a biochemical/haematological test that identifies carriers. From the late 1980s it became possible to screen for carrier status by genetic testing. This was initially by testing for individual mutations such as those in the *CFTR* gene in which mutations predispose to cystic fibrosis. Carrier screening programs were set up in communities at risk of autosomal recessive conditions such as Tay-Sachs disease in the Jewish community, haemoglobinopathies in those from Africa, Asia and Mediterranean regions and cystic fibrosis in Caucasian populations. It is now possible to test people for carrier status for thousands of autosomal recessive and X-linked recessive conditions by next generation sequencing. The federal government has recently funded a project called Mackenzie's Mission where 10,000 couples will be screened for carrier status for over 1000 genetic conditions. Such testing provides choice to couples however it can result in uncertainty and generate ethical concerns.

Proposed Certification Scheme for Medical Laboratory Scientists and Technicians

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[1] *Laboratory Supervisor, Monash IVF, 2 Short Street, Southport QLD. and* [2]*Certification Representative, Scientists in Reproductive Technology (SIRT) subgroup of the Fertility Society of Australia (FSA).*

Background:
In 2017, FSA/SIRT were invited to become involved in the development of a professional certification scheme for medical scientists being led by AIMS and AACB. Two years later and after countless informal and structured consultations, a proposed Certification Scheme has been developed and is ready to be implemented. A large number of stakeholders, although holding sometimes disparate and even conflicting perspectives, reached consensus based on a shared desire to promote the ongoing development of the competence, professionalism and recognition of medical scientists in order for them to continue delivering safe, high quality services to consumers.

Method:
Throughout the consultation process, an agreed position on a number of key elements for the Scheme was established including:

- Accountability and governance
- Entry requirements and Levels to be included
- Standards and methods of competency assessment
- Recertification and maintenance of certification
- Sanctions for not staying competent or breaching conduct codes
- Cost of participation

Results:
The Implementation Plan outlines the final positions reached for each element and outlines the steps required to bring the Scheme to fruition. More detailed work is required for some elements, which will be the task of the Scheme's governance body, to be made up of representatives from ten or more relevant professional associations.

Conclusion:
While participation will be voluntary at the outset, if the Scheme proves its worth to the profession itself and to employers, regulators and consumers, it is likely to become the best benchmark available for assuring competent professional practice. With the preparation of this Implementation Plan, a certification scheme for the medical laboratory scientific workforce is tangibly close.

Managing Stress for Infertility Practitioners and their Patients

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Melbourne Centre for Mindfulness, East Melbourne
www.mcfm.com.au

Background:
The practice of managing infertility brings great rewards but is inherently stressful due to the high stakes involved. Patients are often very anxious and managing their stresses is one of the factors involved in obtaining a successful outcome. Burnout among health professionals is becoming increasingly common and this leads to not only to emotional distress but also has a negative impact on how we care for our patients.
The benefits and the science of mindfulness for both infertility health professionals as well as their patients will be discussed. There is good evidence that mindfulness practice can be an antidote to burnout. Recent studies demonstrate a mindfulness course can improve fertility and diminish depression in couples undergoing invitro fertilization management.
There will be an opportunity to take part in a guided meditation practice.

Management of High-Risk Obstetric Patients

Lindsay Edwards[1]

[1] *Royal Hobart Hospital, Tasmania*

Abstract:
Pregnancy following assisted reproductive technology (ART) may be associated with increased anxiety and management must incorporate a psychological component, in addition to best practice, evidence-based care.

Women with previous pregnancy loss, including early recurrent loss, or a single late miscarriage, appear to be at increased risk of obstetric complications in subsequent pregnancy, even in the absence of medical co-morbidities. Women with significant medical co-morbidities should be offered pre-pregnancy counselling so that they may have a realistic idea of the potential complications (for both mother and baby) and the likelihood of a healthy, uncomplicated pregnancy. Pre-pregnancy counselling allows for an appropriate plan to be made for subsequent pregnancy care, including any necessary adjustment to medication (with the view to ceasing potential teratogens, or continuing medication with increased surveillance) and to encourage conception at a time when the mother's health is optimised (i.e. following a sustained remission in the case of lupus nephritis, or when the HbA1c is within target range in type 1 diabetes mellitus). Women undertaking ART should also be counselled regarding the increased risks (for both mother and baby) of multiple pregnancy.

Women with high-risk pregnancies should have their care individualised, according to their specific condition. These women benefit greatly from continuity of care in a multi-disciplinary setting, with close maternal and fetal surveillance, and timely delivery.

Australians' Understanding of the Decline in Fertility with Increasing Age and Attitudes Towards Ovarian Reserve Screening

Alisha EVANS[1], Sheryl DELACEY[2], Kelton TREMELLEN[1]

[1] *Flinders University, College of Medicine and Public Health, Bedford Park, Australia.*
[2] *Flinders University College of Nursing and Health Sciences, Bedford Park, Australia.*

Background:
Australians have trended towards older parenthood since 1972. Understanding of female fertility is important for informed family planning to avoid difficulty conceiving and adverse infant outcomes.

Aim:
To determine Australians' understanding of fertility decline, discuss factors that influence family planning and explore participants' attitudes towards ovarian reserve testing (ORT). Overall, to suggest necessary changes to assist individuals to consider fertility decline in family planning.

Method:
Survey based analysis of 18-45 year old Australian men and women. Female participants (n=147) gave voluntary responses, sourced through health websites, newsletters and social media. Male participants (n=200) were recruited through Q&A Market Research via paid response.

Results:
Male and female cohorts overestimated the age of female fertility decline. Females believed the decline began at 31 years and males 37 years. Similarly, participants overestimated the effectivity of assisted reproductive technologies. Participants considered the top pre-requisites for having children as having a stable relationship, job security and career progression. Of participants who wanted to have children, 74.12% of women and 34.49% of men said that they would alter their family plans if they received an ORT result indicating premature decline in fertility. Following this, 27.54% of females and 65.63% of males said that, as a response, they would start trying for a family immediately.

Conclusion:
The majority of Australians lack clear understanding of fertility decline and overestimate their ability to conceive. Further education is required about fertility and personalised tests such as ORT may be effective in encouraging women and men to consider their risk of infertility.

“You Can’t Sit With Us” – The Misconception of the Excluded Cell

Tania FERNANDEZ[1], Lynn BURMEISTER[1], Kelli SORBY[1]

[1]*No.1 Fertility, Melbourne, Australia*

Background:
The presence of excluded cells can affect embryo grading and ultimately, its utilisation. The chromosomal aberrations found in excluded cells have created a cynical perception of them.

Aim:
To investigate cell exclusion and its effects on development, euploidy rate (of the remaining embryo) and clinical outcomes.

Method:
A total of 727 embryos, for which 24 chromosome screening data was available, were assessed for evidence of any cell exclusion. The number of cells excluded and the location of cell exclusion (external or internal – within the blastocoel cavity) were recorded for each embryo.

Results:
The patient cohort had a mean age of 38.43 years and a mean of 2.59 blastocysts biopsied. There was no disparity in the rate of euploid embryos when comparing Day 5 and Day 6 biopsy (39.2% and 39.1%).
Cell exclusion was not found to impact the development of embryos, with both the time from syngamy to the start of blastulation and the absolute time taken to reach blastulation not yielding any difference (P=0.30 and P=0.29 respectively).
Embryos with or without excluded cells did not show a difference in euploidy rate, 39.7% and 39.5% respectively. Furthermore, the number of cells excluded, whether 1, 2 or more than 2 cells, did not provide any insight to the ploidy status of the embryo (38.8%, 37.0% and 44.4% respectively; P=0.38). The location of cell extrusion, whether it was external, internal or in both locations, exhibited no difference in ploidy (36.8%, 40.0%, and 51.2% respectively; P=0.10).
While a difference was seen in pregnancy rates of embryos with cell exclusion and those without (45% and 57.4% respectively), this was not statistically significant (P=0.19). The presence or absence of cell exclusion did not change the rate of pregnancy loss (18% and 25% respectively; P=0.75)

Conclusion:
Excluded cells have no detrimental effects on embryo development, euploidy rates and clinical outcomes

The Role of Acupuncture within an Integrative Model of Care for IVF Patients: A Literature Review and Discussion on the Impact Acupuncture May Have on IVF Outcomes and Psychological Well Being of IVF Patients. .

Amy, FORTH[1]

[1]*The Acupuncture Pregnancy Clinic Alexandria, Sydney, Australia*

Abstract:
This presentation discusses the unique role of acupuncture within an integrative model of care of IVF patients in three parts.

Firstly, a review of clinical trials held in Australia and internationally, secondly a translation of trial findings into clinical recommendations for acupuncture during IVF treatment and thirdly, the role of acupuncture within a multidisciplinary and team-based approach to IVF care.

IVF acupuncture research began in 2002 and the most recent publications appeared in January 2019. I shall summarise this research from its beginnings up to the most recent RCT published in 2018 and a 2019 meta-analysis. The significance of treatment dose and timing of acupuncture treatment will be discussed, as will the role of acupuncture in reducing IVF associated stress and anxiety.

Secondly, I will explore how this research may translate into clinical recommendations for acupuncture throughout IVF treatment. This section will also include a short video demonstration of IVF acupuncture.

Finally, the importance of working towards a best practice, team based, patient centered and an integrative approach to care of the IVF patient will be discussed. Multi-disciplinary education, interprofessional communication and shared research platforms are all important components of such a model.

How to Probe Biomolecules Right where it Matters

Ewa M. GOLDYS[1]

[1]*University of New South Wales, Sydney, Australia,*

Abstract:
Our group has been developing new technologies for biomolecular analysis in the living organisms using two separate approaches. The multispectral imaging technique pioneered by our team allows precise quantification of native fluorescent colour of cells and tissues. Uusing a big data approach and building on high processing speeds of modern computers we are now able to unveil the biomolecular composition of cells and tissues. Biomolecules such as NADH, flavins, retinoids, cytochrome C and many others can now be non-invasively monitored. This provides highly sensitive insights into metabolism and its dysregulation. We deployed this method to non-invasively assess the condition of preimplantation embryos where healthy and impaired embryos could be differentiated.

The frontier challenge of understanding the effects of immunity and its regulation requires imaging and detection of low levels of cytokines in living organisms. We introduced novel implantable devices for probing trace levels of secreted cytokines. The ability to assess localized cytokine secretion in living organisms has potential major implications for biomedicine, including in fertility research.

Clinical Benefits of Overnight Insemination Compared to Short Insemination for IVF Patients

Nuria DEZI[1], Natalie HESKETH, Andrew MURRAY, Steven MCARTHUR, Mark LIVINGSTONE, Mark BOWMAN.

[1] *GENEA, Sydney, Australia,*

Background:
Studies suggest that a short insemination protocol for IVF can maintain fertilization rates and increase good quality utilizable blastocysts compared to that of an overnight insemination protocol due to the negative impact reactive oxygen species (ROS) may have on the spermatazoa.

Aim:
To analyze results of a short insemination protocol compared to that of an overnight insemination protocol.

Method:
A retrospective analysis performed at Genea's Sydney clinic between January 2017 and December 2018. A total of 10635 mature oocytes were co-incubated with sperm. In group A, 6171 oocytes were co-incubated for 2 hours; in group B, 4464 oocytes were co-incubated overnight. Rates for fertilization (FR), utilization, good quality utilization and fetal heart pregnancy (FHP) were compared for different age ranges.

Results:
Patients <38 yr in group A had a FR of 60.3% vs 67.9% in group B ($p<0.001$). Patients ≥38 yr in group A had a FR of 59.3% vs 66.5% in group B ($p<0.001$).

Patients <38 yr in group A had a D5/6 utilization rate of 35.5% vs 40% in group B ($p<0.001$). Patients ≥38 yr in group A had a D5/6 utilization rate of 28.1% vs 32.2% in group B ($p=0.0014$).

Patients <38 yr in group A had a D5/6 good quality utilization rate of 27.5% vs 30.1% in group B ($p<0.05$). Patients ≥38 yr in group A had a D5/6 good quality utilization rate of 17.4% vs 19.5% in group B ($p=0.053$)**.**

Similar FHP rates were observed in all groups.

Conclusion:
Extended coincubation of gametes significantly improves fertilization rates and increases the number and the quality of the embryos utilized. Whilst there is no significant improvement in FHP rates, the data suggests that the longer coincubation time does not negatively impact results and may in turn add to laboratory efficiencies.

Oocyte Cryopreservation

Debra GOOK[1,2], Kelly LEWIS[1], Renee HODGSON[1],Boon CHOO[1],and David EDGAR[1]

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[2] *Department of Obstetrics & Gynaecology, University of Melbourne, Parkville, Victoria, Australia.*

Abstract:
In the last decade the outcomes from oocyte cryopreservation have improved significantly with the advent of reproducible vitrification techniques. Extensive application of this approach in large donor oocyte programs has demonstrated that high survival rates can be achieved and that the surviving oocytes can fertilize, develop and implant at rates indistinguishable from those of comparable fresh oocytes. However, when establishing a gold standard outcome for vitrified oocytes from a broader age group and from infertility patients, it is evident that these high outcomes are not replicated, suggesting that variation in outcome may be related to inherent properties of the individual oocytes. There is some evidence to suggest that patient age may influence survival rates but the mechanism by which this could affect survival is unknown. Studies on other parameters which may be implicated, such as abnormalities of the oocyte cytoplasm, oocyte volume and zona pellucida properties, have failed to demonstrate a clear impact on survival but more data are required to confirm this.

An alternative possibility is that these differences in survival relate to technical variation. Our studies have attempted to assess components of the methodology that are likely to impact on vitrification survival. These studies are important in developing an understanding of the critical steps in vitrification and in demystifying the methodology of vitrification for both oocytes and embryos.

Characteristics of Women and their Menstrual Cycle Length and Patterns in a Global Cohort of Women Using a Mobile Phone App

Jessica A GRIEGER[1], Anna TARGONSKAYA[2], Natalia KUKHARCHYK[2], Anna KLEPCHUKOVA[2], Robert J NORMAN[1, 3]

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Background and aims:
There is a surprising lack of current data characterizing menstrual cycle length in healthy women, and the potential differences across demographic and lifestyle variables. The aim is to describe the differences in menstrual cycle length across age, body mass index (BMI), and ethnicity in a global cohort of women using a mobile phone app. This is important for conditions such as PCOS.

Method:
The analysis was run based on the aggregated anonymized dataset from Flo period tracker and ovulation calendar that covers all phases of the reproductive cycle. Self-reported information is documented including demographics, flow and cycle length, ovulation information, and reproductive health and diseases. Data from women aged 18+ years and who had logged 3 cycles (i.e. 2 completed cycles and 1 current cycle) was included (n=1, 579,819 women).

Results:
Of the 1.5 million users, half of those reporting BMI (56.8%, n=202,420) had a normal BMI (18.5-24.9 kg/m^2) and one third overweight/obese. Eighty nine percent of women had a cycle length of 21-35 days. In the older vs. younger age groups (35+ years vs. 18-24 years), there was a higher percentage of older women with a median 27 day cycle length (17.6% vs 9.6%), and a lower percentage with a median 29 day cycle length (10.1% vs. 12.5%). Just over one third of women (n=550,445, 34.8%) self-reported their ethnicity: 18% of Caucasian women had a median cycle length of 28 days compared to 13% of Asian women.

Conclusion:
We provide the most extensive, worldwide, evidence, on the characteristics of women and their menstrual cycle length and patterns. It is the first report on the influence of ethnicity on menstrual cycle length. This information is necessary to support the updating of current clinical guidelines around menstrual cycle length and patterns for clinical use in fertility programs.

High Expectations: What People Think ART can Achieve

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[1] *Victorian Assisted Reproductive Treatment Authority, Melbourne, Australia*
[2] *Public Health and Preventive Medicine, Monash University, Melbourne, Australia*

Background:
Parental age is the most important determinant of the chance of spontaneous and assisted conception. As age of childbearing is increasing, an increasing proportion of the population experience infertility and seek assisted reproductive technology (ART) to conceive. Your Fertility is a government-funded fertility health promotion program to improve awareness in the community about the factors that affect fertility and chance of ART success.

Aim:
To establish reproductive outcomes and understanding of chance of having a baby with ART among people in Australia aged between 18 and 45 years.

Method:
A representative sample of people of reproductive age in Australia were recruited in 2019 (n=716) and asked to complete a telephone interview or an online survey about their fertility-related knowledge and outcomes.

Results:
Just over two in five respondents (42%) had biological children and more than half (56%) wanted to have a child or another child in the future. Almost one third thought that female fertility starts to decline after age 40. Overall, 11% had experienced infertility (been unable to conceive after 12 months or more of trying) and among people aged 35-45 years 18% had experienced infertility. Of those who had experienced infertility 68% had sought medical help. Among female respondents, approximately one in four (23%) indicated that there was some likelihood they would consider freezing their eggs to preserve their fertility. When asked to estimate the chance of having a baby after one IVF attempt for women of different ages, most respondents overestimated this considerably.

Conclusion:
A high proportion of people experience infertility and have unrealistic expectations of what ART can achieve. These findings are used by the Your Fertility program to develop educational material about the impact of age on fertility and ART success and encourage those who need it to seek ART sooner rather than later.

Preimplantation Genetic Testing for Monogenic Disease and Aneuploidy (PGT-M/A) by SNP Genotyping and Karyomapping

Alan H HANDYSIDE[1]

[1]*School of Biosciences, University of Kent, Canterbury, UK*

Abstract:
SNP genotyping and karyomapping is being used increasingly world-wide for linkage-based preimplantation genetic testing of monogenic disease and aneuploidy (PGT-M/A). The ability to genotype a universal set of hundreds of informative SNPs across each chromosome in a single, low cost test has significantly reduced the time and effort required to develop patient and disease specific tests. The use of these markers for high resolution detection of chromosome abnormalities including aneuploidy and structural chromosome imbalance in translocation carriers is also increasing. Unlike quantitative methods of copy number analysis, including array comparative genomic hybridisation (array CGH) and next generation sequencing (NGS), karyomapping identifies the parental origin of these abnormalities. This unique combination of features is providing new insights into the origins and mechanisms behind a range of chromosomal abnormalities in the preimplantation embryo.

Chromosomal Mosaicism and Human Preimplantation Embryo Arrest in Vitro

Alan H HANDYSIDE[1]

[1]*School of Biosciences, University of Kent, Canterbury, UK*

Abstract:
Following *in vitro* fertilisation (IVF), only about half of normally fertilised human embryos develop beyond cleavage and morula stages to form a blastocyst *in vitro*. Although many human embryos are aneuploid and genomically imbalanced, often as a result of meiotic errors inherited in the oocyte, these aneuploidies persist at the blastocyst stage and the reasons for the high incidence of developmental arrest remain unknown. Recently we used genome-wide SNP genotyping and meiomapping of both polar bodies to identify maternal meiotic errors and karyomapping to fingerprint the parental chromosomes in single cells from disaggregated arrested embryos and excluded cells from blastocysts. Combined with time lapse imaging of development in culture, we demonstrateds that tripolar mitoses in early cleavage cause chromosome dispersal to clones of cells with identical or closely related sub-diploid chromosome profiles resulting in intercellular partitioning of the genome. We hypothesise that following zygotic genome activation (ZGA), the combination of genomic imbalance and partial genome loss disrupts the normal pattern of embryonic gene expression blocking development at the morula-blastocyst transition. Failure to coordinate the cell cycle in early cleavage and regulate centrosome duplication is therefore a major cause of human preimplantation developmental arrest *in vitro*.

Naturopathic Support for Patients Undergoing Art: What is the Evidence and how can we Better Collaborate for Patient Outcomes?

Rhiannon HARDINGHAM[1]

[1]*Fertile Ground Health Group, Melbourne*

Abstract:
Clinical experience and research alike indicate that high numbers of patients undergoing ART in Australia seek support from a CAM practitioner, with naturopathic care being one of the most sought after practices. It is also understood that the majority of these patients do not disclose their CAM treatment to their treating specialists (*Rayner, et al.,* 2011). We recognize this as a concern regarding potential treatment outcomes, as well as a potential risk to patient health.

In this presentation we will discuss the scope, safety and benefit of naturopathic support for IVF patients, as well as investigate the evidence to support such lifestyle, nutritional and herbal interventions.

Preconception Screening

Tristan HARDY[1,2]

[1] *Repromed, Adelaide, Australia*
[2] *Genetics and Molecular Pathology, SA Pathology, Adelaide, Australia*

Abstract:
Preconception screening aims to identify couples at risk of having a pregnancy with a single gene disorder. Previously, preconception screening programs were focused on individual genes known to be highly prevalent in particular ethnicities. These programs have had variable success in reducing the incidence of significant paediatric conditions in different communities. Recently, the rapid development of DNA sequencing technologies has caused a rapid evolution of testing options available, and clinical-grade testing for hundreds of single gene conditions is now available to patients via a variety of commercial and public providers. In addition, the Australian government has invested in a research project to address questions surrounding the clinical application of expanded carrier screening in the Australian context. This presentation will address the history of preconception screening, current developments and future opportunities with a focus on reproductive medicine.

Development of an Ovarian Tissue Cryopreservation Protocol

Jennifer PONTRÉ[1,2], Elham AMINI[3], John RYAN[2], Kirsty DOUGLAS[2], Stuart SALFINGER[5], **Roger HART[1,2,4]**

[1] *King Edward Memorial Hospital, Perth, Western Australia*
[2] *Fertility Specialists of Western Australia, Perth, Western Australia*
[3] *Clinipath Pathology, Perth, Western Australia*
[4] *Division of Obstetrics and Gynaecology, University of Western Australia*
[5] *St John of God Hospital, Perth, Western Australia*

Background:
Following a cancer diagnosis, chemotherapy and radiotherapy treatment have the potential to cause loss of future fertility. Vitrification and storage of ovarian tissue for women with a cancer diagnosis may allow post treatment restoration of potential fertility.

Objectives:
To determine the effectiveness of a high quality ovarian tissue cryopreservation and storage protocol, with the objective of establishing an ovarian tissue cryopreservation service to women with a cancer diagnosis at Fertility Specialists of WA.

Methodology:
We performed a double blinded case control study over a 12 month period (2017-2018). Premenopausal women scheduled to undergo laparoscopic ovarian surgery underwent collection of ovarian samples which were halved and randomized as a control ('fresh') specimen, or to vitrification. Tissue assessment was then performed according to published methodology to assess tissue survival post vitrification, and the quality, number, stage and density of primordial, primary and secondary follicles was graded, along with patient demographic data. Ethical approval was granted by the local institutional review board (Ref 1194).

Results:
Of the 4 patients who underwent randomization, mean patient age was 37.7 years (range 35-40). Adequate survival of primordial follicles was recorded in the vitrified samples (mean 83 follicles, range 26-217) when compared to fresh (mean 68.2, range 35-155). A reduction in primary follicle post vitrification was noted (mean 17.5, range 3-34) compared to fresh (mean 21.7, range 8-32), along with a reduction in secondary follicle density post vitrification (mean 0.5, range 0-2) when compared to fresh (mean 1.2, range 1-2).

Conclusion:
Our results show good survival of primordial follicles with reduction of more vulnerable primary and secondary follicles, confirming a lack of a substantial detrimental effect of the vitrification process. This presence of viable follicles post vitrification supports the implementation of an ovarian tissue cryopreservation program for fertility preservation, for women facing a cancer diagnosis in WA.

Impacts of Lifestyle, and Genetics and the Environment

Roger HART[1,2]

[1] *Division of Obstetrics and Gynaecology, University of Western Australia, Australia'*
[2] *Fertility Specialists of Western Australia,*

Abstract:
This rather ambitious titled talk will attempt to provide an overview of the early life influences of the maternal environment on reproductive outcomes, and will also discuss the potential influences of environmental exposures on reproduction.

Mitochondria: More than ATP

Alexandra J. HARVEY[1]

[1] *University of Melbourne, Parkville, Australia,*

Abstract:
For decades, mitochondria have primarily been regarded as companion organelles that merely fulfil the energetic requirements of a cell to maintain homeostasis. However, mitochondria are dynamic organelles that are also active participants in the regulation of signal transduction pathways through the production of reactive oxygen species, calcium and other molecules. Coordinated communication between not only the nucleus and mitochondria, but also other organelles, is essential for mitochondrial function.

In addition to changing energy demands, mitochondria undergo dynamic, stage-specific restructuring and redistribution during oocyte maturation and preimplantation embryo development, necessary to support key developmental events. Perturbations and deficits in mitochondrial function manifest not only as reduced quality and/or poor oocyte and embryo development but contribute to post-implantation failure, downstream cell function and adult disease. This has long been attributed to their roles in generating ATP, however more recently it has become evident that metabolites function as signaling molecules in their own right. A growing body of evidence, particularly from stem cells, indicates that altered availability of mitochondrially-derived metabolic co-factors modulate the activity of epigenetic modifiers to alter cell lineage decisions. Consequently, oocyte and embryo mitochondrial activity and dynamics have the capacity to establish long-lasting alterations to the epigenetic landscape.

Rather than simply being perceived as the power plant of our cells, mitochondria play essential roles in sensing and communication of cellular function, and act as a conduit between the cytosol and nucleus. Hence, mitochondrial integrity, communication and metabolism are critical links between the extracellular environment, the epigenome and the regulation of embryo development.

Previous Miscarriage and Ectopic Pregnancy – A Case Series Supporting Luteal Phase Defect

Tim HASTED[1,2] and Lucas McLINDON[2,3]

[1] *Queen Elizabeth II Jubilee Hospital, Brisbane, Australia*
[2] *School of Medicine, University of Queensland*
[3] *Mater Mothers Hospital, Brisbane, Australia*

Background:
Luteal Phase Defect (LPD) is an enigma in the pathophysiology of infertility, if indeed it is a significant clinical entity[1]. It remains undefined, with an unknown incidence and controversy surrounding whether it is a cause of infertility and early pregnancy loss. While various methods for determining such a defect have been proposed, including endometrial biopsy and integrated progesterone profiles, many feel that such efforts for diagnosis are not justified[2]. The key hormonal marker is a relative inadequacy of progesterone. We know progesterone in the luteal phase is responsible for tubal peristalsis, and maturation of the endometrium for successful implantation[3,4]. Previous research has suggested an association between LPD and ectopic pregnancy in subfertile women[5].

Research Aims/Objectives:
To identify whether nulliparous patients with a history of both miscarriage and ectopic pregnancy had different rates of LPD compared to other subfertile patients.

Methodology:
Using prospectively collected data in an Australian public hospital infertility clinic, the obstetric history of over 600 women experiencing infertility or recurrent miscarriage were collected. All women undertook a timed series of luteal hormonal profiles of serum oestradiol and progesterone and published LPD criteria were applied[6].

Results/Findings:
We found an LPD exists in under 40% of women who presented to our clinic. In the subgroup of nulliparous women with a history of miscarriage and ectopic pregnancy LPD is present in over 80% of cases.

Conclusions:
LPD may impact the successful transport of the conceptus and ongoing intrauterine early pregnancy. There appears to be an association between prior miscarriage, ectopic pregnancy and LPD in subfertile couples. An intervention trial could be considered, providing hormonal support for those experiencing LPD with a history of only unsuccessful pregnancies.

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Investigation of Contamination in the Clinical IVF Laboratory

Natalie HESKETH, Genevieve RUSDEN, Steven MCARTHUR, Mark BOWMAN

Background:
There is an ongoing concern of increased antibiotic resistance for various forms of bacteria. This concern does not stop at just the human level; considerations must be made as to the impact that this resistance may have at the embryonic level in a clinical IVF laboratory. Whilst contamination events are rare they are on the increase and laboratories need to be prepared to react swiftly. However of perhaps more importance is to maintain a continued focus on the prevention of such contaminations.

Aim:
To document essential measures clinical IVF laboratories should have in place to prevent contamination events and steps to take if such events were to occur.

Methods:
Using a number of isolated contamination events across multiple laboratories from 2012 through to present, we have documented type, source, resistance and severity of bacterial contamination. Using this information we have streamlined our response and documented areas of concern of possible sources and improved our aseptic techniques to minimize such outbreaks.

Results:
Introduction of timelapse systems allows for the earlier recognition of contamination and allows for isolation to prevent further spread. Sampling of culture media as well as spare control media from the same source/lot is essential for bacterial identification and sensitivity to certain antibiotics. Swabbing of females and testing of males is recommended, however due to natural flora may be inconclusive. Use of aseptic techniques whilst preparing culture media dishes, gloves, handwashing and general personal health are all areas that need to have a continual focus.

Conclusions:
Contamination events in the IVF laboratory can be devastating and are on the increase. It is essential for IVF laboratories to document contamination events and investigate type and the source of the contamination to allow for the underlying cause to be eliminated has quickly as possible and to put measures in place to prevent reoccurrence.

Is IUI for Unexplained Subfertility Value for Money? An Economic Analysis.

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Background:
One in six couples in Australia experiences fertility problems[1]. Even though randomised clinical trials have confirmed the effectiveness of intra-uterine insemination (IUI) as compared to IVF in couples with unexplained subfertility, IUI, while much less expensive than IVF, is used on a limited scale in Australia.

Aim:
We aim to elucidate what is the cost-effectiveness of IUI compared to IVF with as a first-line treatment in couples with unexplained subfertility in Australia.

Method:
We performed a retrospective cohort analysis among consecutive couples who had unexplained subfertility and underwent IUI in a single fertility centre between January 2013 to December 2017. Couples were followed from the start of IUI until live birth (registered at the moment of conception), or the last cycle of IUI. We calculated cumulative live birth rates with four cycles of IUI and their actual out-of-pocket costs. We extracted cumulative live birth rates after two cycles of IVF (40%) from an optimistic estimation made by Beth A. Maliza et. al.[2] We assumed each cycle of IVF costs $5000 AUD from the couple which reflects the general condition in Australia. We computed the mean costs of IUI and IVF for each live birth respectively.

Results:
Overall, for 574 couples with unexplained subfertility the cumulative chance to have a live birth by undergoing 4 cycles of IUI was 21% (95% CI 16%-27%). The mean out-of-pocket costs for each live birth of a child were $16626 AUD for four cycles of IUI and $25000 AUD for two cycles of IVF (mean difference -$8374 AUD).

Conclusion:
Compared with two cycles of IVF, four cycles of IUI had a better cost-effectiveness in achieving live birth. The value of IUI in treating unexplained subfertility, with low cost and minor safety concerns, should be reconsidered in Australia.

Reference

[1]Australia National Women's Health Policy: Fertility and Infertility. The Department of Health. Last updated: 7th February 2011 (http://www.health.gov.au/internet/publications/publishing.nsf/Content/womens-health-policy-toc~womens-health-policy-experiences~womens-health-policy-experiences-reproductive~womens-health-policy-experiences-reproductive-maternal~womens-health-policy-experiences-reproductive-maternal-fert)

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IUI for Unexplained Infertility - The Lost ART

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Background:
One in six couples in Australia experiences fertility problems[1]. Randomized clinical trials have confirmed the effectiveness of intrauterine insemination (IUI) as compared to no treatment and IVF. However, IUI, while much less expensive than IVF, is used on a limited scale in Australia.

Aim:
To study, in women with unexplained subfertility, the cumulative chance of conception leading to live birth from intrauterine insemination (IUI).

Method:
We performed a retrospective cohort analysis among consecutive couples with unexplained subfertility in a single fertility centre from January 2013 to December 2017. Couples were followed from the start of IUI until live birth (registered at the moment of conception), or the last cycle of IUI (up to 8 cycles). We constructed Kaplan Meier curves and estimated cumulative live birth rates with IUI in terms of days since IUI and number of cycles.

Results:
In total, 574 couples with unexplained subfertility underwent 1313 cycles of IUI. The median age of women included in this study was 35 (range 21 to 45). Of all the women in the study, 11.71% of them had previous pregnancy over 20 weeks gestation, whereas the remainder of 88.29% women did not. The cumulative chance of conception leading to live birth within 90 and 180 days from IUI treatment was 18% [95% confidence interval (CI) 14%-23%] and 24% (95% CI 18%-31%), respectively. Similarly, the cumulative chance to have a live birth by undergoing three and five cycles of IUI was 19% (95% CI 15%-24%) and 24% (95% CI 17%-35%), respectively. The chance did not further increase with more cycles of IUI performed.

Conclusion:
Couples with unexplained subfertility have a reasonable cumulative chance of live birth by having five cycles of IUI within 180 days. The value of this treatment in treating unexplained subfertility, with low cost and minor safety concerns, should be reconsidered in Australia.

Reference:
1 Australia National Women's Health Policy: Fertility and Infertility. The Department of Health. Last updated: 7th February 2011 (http://www.health.gov.au/internet/publications/publishing.nsf/Content/womens-health-policy-toc~womens-health-policy-experiences~womens-health-policy-experiences-reproductive~womens-health-policy-experiences-reproductive-maternal~womens-health-policy-experiences-reproductive-maternal-fert)

Comparing the Cumulative Live Birth Rate from Autologous and Donor Oocytes in Women 40 years and Above: A Retrospective Population Study by Discrete-Time Analysis.

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Background:
Cumulative live birth rates (CLBR) are a better measure of the chance of success of assisted reproductive technology (ART) treatments than cycle-based rates. There is limited population-based information on the CLBR of women using their own oocytes, compared to women of a similar age, using donor oocytes.

Aim:
The aim of this study was to determine the CLBR for women ≥40 years, undergoing ART using autologous oocytes, compared to women of similar age using donor oocytes.

Method:
A population-based retrospective cohort study was conducted using Victorian Assisted Reproductive Treatment Authority (VARTA) data from 2009 to 2015. Data was analysed from all women aged ≥40 years who received ART using only donated oocytes (n=987) or only autologous oocytes (n=19 170). Women were grouped by treatment type (autologous or donor oocytes) and age (40, 41, 42, 43, 44, 45, 46 and ≥47). The primary outcome was CLBR. A live birth was defined as a baby showing signs of life with gestational age ≥20 weeks or birthweight ≥400 grams. A discrete-time survival model was used to evaluate the CLBR. Women were followed up until a live birth was achieved or until 30th June 2016.

Results:
The overall CLBR for women using donor oocytes was 20.2% compared to 5.5% for women using their own oocytes. The discrete-time survival analysis demonstrated significant odds ratios on CLBR across all ages (range OR: 2.56, 95% CI: 1.62–4.01 to OR: 15.40, 95% CI: 9.10–26.04). The number needed to treat (NNT), across all ages was seven (95% CI 6-8).

Conclusion:
Women aged ≥40 years, using donor oocytes had a significantly higher CLBR than women using their own ooctyes. The findings can be used when counselling women ≥40 years about their ART treatment options and to inform public policy.

Endometritis and Infertility

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Abstract:
Endometritis is an infectious and inflammatory disorder of the endometrium with two histological subtypes: acute and chronic. In contrast to the acute presentation, chronic endometritis is often poorly recognized by patient and clinician due to the subtle and non-specific nature of symptoms if any are present.

Most commonly, chronic endometritis is caused by microbial infection. The true prevalence is difficult to determine due to differences in reported populations, sampling methodology and analysis but is thought to be between 8 and 72 percent. Histological assessment of biopsy samples, hysteroscopic visualisation of the endometrial appearance, microbial culture and more recently molecular microbiology utilising next generation sequencing are all described diagnostic methods however concordance between these methods is poor.

It is believed that the inflammatory process results in altered endometrial receptivity and therefore has a role in otherwise unexplained infertility, recurrent pregnancy loss and or recurrent implantation failure. Oral antibiotics are believed to represent a safe and efficacious treatment for chronic endometritis but optimal dosing and regimens are yet to be determined. There is a need for further well designed trials to determine the optimal sampling methodology and diagnostic criterion, treatment regimen and role of these in the evaluation and treatment of infertility.

The Uterine Microbiome

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Background:
The microbes in the reproductive tract, especially the vagina, have long been known to be associated with the health status. Dysbiosis of the microbiome is associated with symptoms and conditions such as bacterial vaginosis, and also a risk factor for sexually transmitted infections. Recent evidence suggests there is an integral interplay with the microbiome and the local host cellular responses. Hence, the microbiome of the uterine environment is likely to also critically interplay with the local tissue cellular response, potentially impacting on fertility treatment outcomes.

Aim:
The aim of this research was to explore the endometrial microbiome, local cellular response in the form of gene expression and metabolic profiles. Secondary insights into if these profiles and data correlate with fertility status and eventually fertility treatment are the ultimate aims of the project.

Method:
Participant bio-specimens from women with informed written consent, and human research ethics approval were collected from women attending for infertility care and women attending for other reasons. Specimens were analysed using next generation sequencing protocols, PCR protocols, and data analysis from participant data.

Results:
Certain microbial members and compositions may be associated with distinct profiles of gene expression and may be associated with and women experiencing infertility. These data require further analysis and replication in additional samples sets.

Conclusion:
The microbiome may be a future element of consideration for infertility treatment, but further work is needed before this possibility becomes a reality.

Advanced Glycation End-Products & the Developing Embryo: Physiological Effects of Dietary Factors Associated with Obesity on Preimplantation Embryo Development

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Background:
Obesity is a global pandemic: 63% of Australians are overweight or obese. Critically, approximately 30% of Australian women are obese before conception (AIHW). Obesity reduces natural and IVF pregnancy success, and increases miscarriage & preeclampsia risk. 'Toxic' Advanced Glycation End-Products (AGEs), formed when reducing sugars react with the free amino group on proteins, are elevated four-fold in uterine fluid of obese, infertile women versus lean women.

Aim:
To examine if AGEs, equimolar to those within the uterus of obese women, impact development and function of preimplantation embryos.

Method:
Preimplantation mouse embryos were cultured with AGEs equimolar with uterine concentrations from lean vs. obese women.
1) AGEs receptor (RAGE & TLR4) immunolocalisation, & TUNEL staining (apoptosis assessment), investigated potential mechanisms of AGEs action on embryo development;
2) Developmental morphokinetics assessed by time-lapse microscopy (Embryoscope);
3) Trophectoderm and inner cell mass cellular allocation determined by differential staining;
4) Implantation potential assessed by blastocyst outgrowth assay;
5) AGEs targeting drug metformin used to ameliorate AGEs mediated effects.

Results:
Preimplantation embryos express RAGE & TLR4, providing a mechanism for AGEs-mediated signaling. "Obese" AGEs significantly reduced blastocyst hatching rates (50%, $p<0.0001$) and embryonic cell-proliferation, supported by absence of TUNEL-staining and delay in morphokinetic embryo-development (~3-hour lag). AGEs reduced blastocyst cell number (24%, $p<0.0001$), specifically in the trophectoderm (23%, $p<0.001$). Blastocyst outgrowth, an indicator of implantation potential, appears to be compromised by "obese" AGEs. Metformin treatment reduces AGEs mediated effects on embryo development by preventing reduction in trophectoderm cell number.

Conclusion:
Elevated uterine AGEs are likely detrimental for fertility. AGEs equimolar to the obese uterine environment detrimentally affect early mouse embryo development, blastocyst hatching, and implantation potential, providing a physiological link between obesity and reduced fertility. Metformin may overcome these effects, and provides a potential therapeutic option to improve embryo development in obese infertile women.

Meta-Analysis: Is it the Platinum Standard of Evidence

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Abstract:
Evidence-based practice (EBP) involves the application of the best available research evidence to clinical expertise and patient values. The term ‘best available evidence’ can be interpreted according to the ‘evidence hierarchy’, which places systematic reviews at the top. This presentation will explore how systematic reviews are constructed, explore the use of meta-analyses, and how such evidence can be utilized in the EBP paradigm. It will explore the strengths and limitations of systematic reviews, from both theoretical and practical viewpoints. Specific aspects to be explored will include how to structure the clinical question, construct a search strategy, perform the critical appraisal of information and synthesis of quantitative data. It will also explore the value of meta-analysis, and whether systematic reviews should only be limited to randomized controlled trials. Finally, we will explore how systematic reviews can best be used in the field of fertility.

Should Australian Men be Concerned About Their Biological Clock?

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Background:
As the biological age of first-time parents is rising, investigation of increased male age on fecundity parameters will provide a better understanding of cumulative effects of leaving childbearing to an older age. Studies [*Fertility and Sterility*, **75** ,2 (2001); *Reviews in Urology*, **13**, 4 (2011)] suggest sperm motility and DNA fragmentation (DF) deteriorate with male age however the link with sperm concentration is the least consistent.

Aim:
To determine the effect of male age on total sperm count (TSC), total motility (TM) and DF of males attending an Australian fertility clinic.

Method:
Over 39 000 semen tests performed at Genea (2009 to 2019) were split into age groups (<30, 31-35, 36-40, 41-45 and >45) and retrospectively analysed, assessing TSC (reference range >39 million/ejaculat) and TM (reference range >40%) following the WHO Laboratory Manual 4th/5th and DF (reference range <29%), using a validated in-house method (Sperm Chromatin Integrity Test).

Results:
TSC was significantly ($p<0.05$) lower in the >45 age group (170 million/ejaculat), with the lower age groups having a TSC of 201, 215, 211 and 202 million/ejaculat, respectively. Similarly, TM of the >45 age group (54%) was significantly lower ($p<0.05$) than the TM of lower age groups, with values of 61%, 61%, 60% and 59%, respectively. A significant ($p<0.05$) DF increase was observed in the >45 age group, with an average DF of 18%, in contrast to all other age groups with DF of 12%, 12%, 13% and 14%, respectively.

Conclusion:
It is assuring to Australian men and fertility practitioners that this reduction in the semen parameters of the over-45 male are still well above the normal WHO ranges. However, male age is beginning to be an important factor to consider in addition to the already known impact that female age has on a couples' fecundity.

Tangible Benefits of PGT-A

Mandy KATZ-JAFFE[1]

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Abstract:
Aneuploidy, defined as the loss or gain of a chromosome, is the leading cause of implantation failure, miscarriage and congenital abnormalities in human conception. Chromosome aneuploidy is directly associated with advanced maternal age and is responsible for a significant portion of observed reproductive failure for older women undergoing infertility treatment. It is well known that for women in their forties, the proportion of aneuploid oocytes increases dramatically resulting in up to 75% chance of pregnancy loss due to chromosome aneuploidy. This high frequency of aneuploidy and its adverse impact on a successful reproductive outcome has led to the development of preimplantation genetic testing for aneuploidy (PGT-A) as an embryo selection technique to identify chromosomally normal (euploid) embryos during an IVF cycle. Randomized control trials, retrospective cohorts and meta-analyses comparing PGT-A based embryo selection with standard embryo morphological assessment have observed significantly improved outcomes in a shorter time frame for patients undergoing infertility treatment. Euploid embryos were more likely to successfully implant with the utilization of PGT-A based embryo selection compared to standard morphological assessment thereby resulting in higher ongoing clinical pregnancy and live birth rates, alongside decreases in miscarriage rates and multiple gestations. With a significant reduction in the likelihood of an adverse outcome including implantation failure and miscarriage, patients are less likely to be exposed to the physical and emotional burden of IVF failure or pregnancy loss. PGT-A based embryo selection has been shown to contribute to a shorter time frame to a live birth and the potential for a more patient friendly approach.

How Long is a Piece of String, Time to Pregnancy?

Mandy KATZ-JAFFE[1]

[1]*CCRM Fertility, Colorado, USA,*

Background:
The ability to select the most competent embryo for transfer is critical to the success of infertility treatment and has the potential to shorten time to pregnancy and live birth. Preimplantation genetic testing for aneuploidy (PGT-A) has been proposed as an improved embryo selection strategy.

Aim:
In a time-to-pregnancy analysis, beginning at initial physician consult, we prospectively investigated, in a maternally age-matched cohort, clinical outcomes with PGT-A compared to freeze-all blastocyst cycles with embryo selection based on morphologic grading alone.

Method:
Infertile couples were identified during their initial IVF consult as intent to treat with either a freeze-all blastocyst cycle or IVF with PGT-A. Female patients were maternally age- matched between the two treatment groups (mean 32.5 ±3.7 years; n=46 per group) and presented with comparable infertility diagnoses without significantly compromised ovarian reserve. For the 'Freeze All' group, blastocysts were vitrified using the Cryotop method on either day 5 (D5) or day 6 (D6) of development. In contrast, for the 'PGT-A' group, prior to vitrification, D5 or D6 blastocysts were biopsied and analyzed for chromosome numeration using the VeriSeq™ platform (Vitrolife). Standard protocols for a hormone replacement frozen embryo transfer (FET) were utilized for patients in both treatment groups, with either embryo selection based on blastocyst morphology alone (Freeze All) or a combined euploid and morphology result (PGT-A). Primary outcomes measured included implantation (fetal heart tone, FHT), miscarriage, and live birth rates, significance at $P<0.05$.

Results:
In each treatment group, 46 retrievals were performed with no significant differences in number of oocytes retrieved, fertilized, number of usable blastocysts blastocyst cryo-survival between the two treatment groups ($P\geq0.05$; ns). Two retrievals (4.4%) resulted in no fertilization and four (8.7%) with no blastocyst development in the Freeze All group, while one (2.2%) resulted in no fertilization and four (8.7%) with no blastocyst development in the PGT-A group ($P\geq0.05$; ns). Additionally, following PGT-A, two (4.4%) cycles ended with all aneuploid blastocysts. A total of n=39 PGT-A and n=40 Freeze All patients underwent their first FET with a comparable number of embryos transferred (ns). Clinical outcomes were significantly improved following embryo selection with PGT-A and morphological grading combined; including implantation rate +FHT (78.9% PGT-A vs 48.2% Freeze All; $P<0.0001$), live birth rate from first FET (79.5% PGT-A vs 50.0% Freeze All; $P<0.01$) and live birth rate from intent to treat (65.2% PGT-A vs 43.5% Freeze All; $P<0.01$). A trend towards lower miscarriage was also observed in
the PGT-A group (6.1% PGT-A vs 16.7% Freeze All; ns). The intent to treat selection and transfer of a euploid blastocyst in this maternally age-matched prospective cohort study resulted in approximately 25% more patients delivering chromosomally normal babies ($P<0.01$).

Conclusion:
From the prospective of intent to treat analysis, at the time a clinical decision is made to proceed with IVF therapy, the inclusion of PGT-A and morphology grading combined resulted in significantly improved clinical outcomes in a maternally age-matched population. These improvements resulted in the fastest time to pregnancy and live birth following the first embryo transfer for women pursuing IVF.

How Much is a Human Life Worth? A Systematic Scoping Review in the Context of Fertility Treatment

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Background:
How society and governments value fertility treatment is fundamentally different to other areas of healthcare. Infertility is valued on its ability to create new life, while most other types of healthcare are valued on their ability to save, extend or improve existing life. A number of fields assign monetary values to a human life – whether these methods are appropriate for valuing fertility treatment is a new field of research.

Aim:
The aim of this systematic review was to explore the methods used to elicit the value of a human life and to describe the settings these are used in as well as their strengths and limitations.

Method:
We performed a systematic review of the peer-reviewed literature between 2009 and 2019 to identify methodological and empirical studies concerned with elicitation methods for valuing a human life regardless of the context (i.e. health, environment etc.). We critically appraised the elicitation method used, the discipline, strengths and limitations of the method.

Results:
The initial search strategy identified 1,814 potentially relevant studies. Stated preference methods such as contingent valuation and choice experiments are significantly more common than revealed preference studies (e.g. using compensating wage differentials). The majority of literature elicits values of a human life in the context of developed countries, and value a statistical life rather than a statistical life year. Estimates for the value of a life vary substantially depending on the approach used, with values ranging from <US$10M to >US$700M for developed countries. In the presentation I will summarize methods used in more detail and highlight their strengths and limitations.

Conclusion:
There is a number of different approaches to elicit the value of a human life, some of which are relevant to fertility treatment. Health technology assessment agencies should be open to such methods for the evaluation of fertility treatment.

What Role do Australian Fertility Clinics Play in Donor Linking?

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Abstract:
A growing number of donor-conceived adults and parents of donor- conceived children are seeking to identify their sperm donor and/or donor siblings. In three Australian states, legislation provides donor-conceived children with access to their donor's identity when they reach 16 (WA) or 18 (Victoria & NSW). In Victoria, parents of donor-conceived children who are still minors can request the donor's identity, which will be released if the donor consents. In these states, a government department or statutory authority facilitates linking. In the remaining states and territories there are no formal mechanisms for donor linking. As a result, donor-conceived adults and parents often turn to their fertility clinic for information. Drawing on qualitative interviews with fertility clinic staff from across Australia, the paper reports on the nature and extent of clinic-facilitated donor linking. In the absence of legislative access to information, we found that a significant number of fertility clinics are facilitating donor linking of some kind, including retrospective linking where the donor donated under conditions of anonymity. However, clinic staff often felt unsure about what information could be released and did not always have the resources to adequately manage the linking process. The research suggests that uniform donor linking legislation, administered by a statutory authority, is needed in every state.

A Prospective Randomized Controlled Trial of GnRH Agonist in the Luteal Phase of an Antagonist Cycle (GALA trial)

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Background:
GnRH agonist administration in the luteal phase of an IVF cycle has been proposed to be beneficial in increasing pregnancy rate and livebirth rate.

Aim:
To determine if administration of a single dose the GnRH agonist leuprorelin on day 6 of the luteal phase increases pregnancy rates

Method:
In a prospective, computer ramdomised double blinded trial, patients age between 18 and 42 years old who underwent their first IVF cycle at The Fertility Centre, Queensland were recruited to take part in the study. The IVF protocol was standardized to a low dose antagonist cycle, trigger with recombinant HCG and vaginal progesterone for luteal phase support. Only single embryo transfers are eligible for the study. Patients were randomized to receive 0.5mg leuprorelin or placebo on the sixth day post oocyte retrieval.

Results:
A total of 177 patients were recruited for the study, ninety received leuprorelin and eighty seven received placebo. There was no difference in terms of age, BMI and baseline AMH among the leuprorelin group and the placebo group. There was no difference between pregnancy rate (34.4% vs 36.8%, P>0.05) or live birth rate (28.9% vs 27.6%, P>0.05) between the two groups

Conclusion:
Administration of single dose leuprorelin in luteal phase of an IVF cycle does not increase the pregnancy and livebirth rate in this study

IVF After Renal Transplantation: A Literature Review of Cases

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Background:
Chronic renal disease affects fertility. After renal transplant, hypothalamus-pituitary-ovary (HPO) axis function may resume, where ovulation and spontaneous pregnancy may occur. In some cases, however, IVF is required. There is no published systematic review of results of IVF after renal transplantation, a group that can be considered high-risk for maternal, transplant and fetal outcomes.

Aim:
To describe the published cases of IVF pregnancies after renal transplantation, with regard to patient demographics, immunosuppressive medication regimen and birth outcomes.

Method:
Literature review of cases and analysis of existing studies. MeSH (medical subject heading) terms 'Fertilization in vitro' AND 'kidney transplantation', and related words, were searched on PubMed and Google Scholar.

Results:
Worldwide over 30 cases of pregnancies were identified from 1995 to current time, from case reports, hospital units and registry data. An Australian database reported IVF in 3 women that resulted in 4 pregnancies and 5 live births, of a total 447 pregnant renal transplant recipients. (Wyld)

Conclusion:
IVF in female renal transplant recipients is achievable, with attention required to improve affected outcomes such as hypertensive disease, birth weight and gestation. Considerations also to the pelvic transplanted kidney in oocyte pick-up, risk of infection and mode of delivery. Publication bias may exist, as the denominator of attempted IVF cycles is not fully reported. Ethical considerations include patient reproductive autonomy alongside the potential for shortened maternal life expectancy, dependent on aetiology of the original kidney disease. More research is needed to determine factors that affect success, risks and supports for women and their families if they choose IVF after renal transplantation.

References:
Wyld ML, et al. Pregnancy outcomes for kidney transplant recipients. Am J Transplant. 2013 Dec;13(12):3173-82.

Cytological Analysis of Sperm Penetration and Arrest of Fertilization in Mature Oocytes that did not Form Pronuclei Following Conventional IVF

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Background:
Unfertilized oocytes after conventional IVF (c-IVF) may fail to form pronuclei due to lack of sperm penetration. For c-IVF failed patients, intracytoplasmic sperm injection (ICSI) is the only hope for pregnancy. However, ICSI may not result in fertilization, even though sperm is definitely injected. Although ICSI has been investigated extensively, few reports on unfertilized oocytes after c-IVF have been published.

Aim:
To analyze sperm penetration and arrest of fertilization in mature oocytes that did not form pronuclei following c-IVF.

Method:
Unfertilized mature oocytes (n=64) without pronuclear formation within 44 hours after insemination by c-IVF were donated. We conducted a cytological analysis of the donated oocytes, using immunofluorescent staining with anti-pericentrin antibody as a marker of centrosomes to examine sperm penetration. Microtubules and DNA of the oocytes were identified using an anti-alpha tubulin antibody and Hoechst 33342, respectively. Images were obtained using an FV1000 confocal microscope.

Results:
Out of the 64 unfertilized mature oocytes, 50 showed a double-positive signal for DNA and alpha tubulin in the ooplasm, which was thought to indicate the metaphase spindle of the second meiotic division. In addition, there was no pericentrin signal, suggesting that sperm penetration did not occur. On the other hand, three oocytes showed pericentrin signals, suggesting that sperm had successfully penetrated. Two of these three oocytes may have arrested during formation of the sperm aster. Interestingly, the other oocyte showed two pericentrin signals at the poles of the assembled spindle. The male and female chromatin in this oocyte may have fused without forming pronuclei, with development thus arrested before the first cleavage. The remaining 11 oocytes showed two spindles without pericentrin signals in the ooplasm, although the reason for this was unclear.

Conclusion:
We found that most unfertilized c-IVF oocytes lacked signs of sperm penetration. However, fertilization begun and then arrested after sperm penetration in some oocytes.

Use of Electronic Witness Systems in IVF Laboratories Decreases Incidents Whilst Increasing Compliance in Reporting Near Misses

Kristy LAMERTON, Natalie HESKETH, Samantha SIMPSON, Mark BOWMAN, Steven MCARTHUR

Background:
Traceability of samples is of utmost importance in IVF laboratories. Due to the highly repetitive microscopic nature of the work that is performed it is remiss to assume that mistakes do not happen and as such it is the responsibility of clinic managers to put strategies in place to reduce such errors.

Aim:
To ascertain the benefit of an electronic witnessing system for reducing risk in the clinical ART laboratory and increasing compliance in reporting near misses.

Method:
A retrospective comparison using a risk database of recorded incidents and near misses across Genea IVF laboratories. A period of 3 years using a manual ID checking system (2012 – 2014) was compared to a period of 3 years using a fully integrated electronic barcode identification system (2016 – 2018) (Gidget, Genea Biomedx, Sydney).
Data was categorized into Near Misses (NM) for those events that the ID checking picked up on an error prior to samples being transferred to the wrong vessel or dish, and Incidents (I) which the ID checking system failed and resulted in movement of samples to incorrectly labelled vessels or to the point of being introduced into a clinical procedure room.

Results:
Genea laboratories perform upwards of 5000 OPU cycles and 3500 cryo cycles across all their clinics annually. With these procedures combined there is on average 7 ID check points for each procedure totaling over 175,000 separate ID check points over each 3 year period. For the period of manual ID checking there were 7 near misses reported and 8 identification incidents. For the period since full integration of the electronic barcode identification system there were 85 near misses reported and 1 identification incident. In both time periods there has never been an RTAC reportable incident.

Conclusion:
The use of electronic witnessing systems has the ability to significantly reduce identification errors in the workplace whilst increasing reporting of near misses. This captures potential hazards and prevents more serious events from arising.

Is More Always Better? Female Age Modifies the Oocyte Number Where Maximal Cumulative Live Birth Rate per Aspiration Is Observed: An Analysis of 221,221 Cycles.

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Background:
Live birth rate per fresh or frozen embryo transfer (FET) has traditionally been the primary measure of assisted reproductive technology (ART) success. However, with the introduction of highly efficient embryo cryopreservation methods, cumulative live birth rates (CLBR) encompassing live delivery outcomes from the fresh and all subsequent FET following a single ovarian stimulation is increasingly viewed as a more meaningful measure of treatment success. There is growing evidence suggesting that larger oocyte yields are associated with higher CLBR. Whether this association is uniform across female ages has not yet been properly explored.

Aim:
To assess the number of oocytes retrieved where maximal CLBR was observed in women of different ages.

Method:
This is a large retrospective population-based cohort study using data from the Australian and New Zealand Assisted Reproduction Database (ANZARD). Overall, 116,677 women undergoing 221,221 autologous cycles between January 2009 to December 2015 were included in the analysis. Generalised estimating equations were used to account for the clustered nature of data. An interaction analysis was performed to assess the effect-modifying role of female age.

Results:
The CLBR for women aged <30 and 30-34 years appeared to reach a plateau at 73% after retrieval of 25 oocytes. The CLBR of women aged 35-39 and 40-44 years continued to increase with higher oocyte yields, reaching 68% and 40% respectively when >30 oocytes were retrieved. The CLBR of women aged ≥45 peaked at around 9 oocytes, remaining consistently below 5%. Trends in CLBR and oocyte numbers differ by age, with lower rates of increase in CLBR per additional oocyte retrieved in the older age groups.

Conclusion:
More is not necessarily always better. Findings suggest that the number of oocytes retrieved where maximal CLBR is observed is around 25 in women 18-34 years, >30 in women between 36-44 years and around 9 in women ≥45 years.

Culture of Embryos in the Embryoscope® Increases Blastocyst Formation and Quality and Resultant Fetal Heart Rate Compared to Minc™ Benchtop Incubator

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[1] *Melbourne IVF, Melbourne, Australia*

Background:
Over the past 5 years, there has been an increase in the use of time-lapse incubator systems, which allows for continuous monitoring of embryos. As such, time-specific morphological changes can be determined and embryo selection software applied to select the best embryo for transfer. However, there has been considerable debate in the literature over the benefits of such systems and a recent review of 8 randomized controlled trials (Armstrong et al., 2018) was inconclusive. Crucially, interpretation and comparison of results are complicated by differences among imaging systems and variations in culture protocols.

Aim:
The aim of this study was to investigate, from a single-centre ART unit, the rates of blastocyst formation and quality, as well as subsequent pregnancy rate from fresh embryo transfers between embryos cultured in the Embryoscope and MINC incubators.

Method:
Retrospective data from 1189 Embryoscope cycles and 1381 MINC cycles conducted concurrently were collected, using Vitrolife G-TL media under 5% O_2.

Results:
There was an increase in day 5 top quality blastocysts (Gardner grading 'AA') from embryos in the Embryoscope compared to the MINC (15.3% vs.9.7%,$p<0.0001$), and day 5 good quality blastocysts (≥'BB', 24.4% vs.16.9%,$p<0.0001$). Overall, the utilization rate was significantly higher from embryos in the Embryoscope (51.3% vs.46.0%, $p<0.0001$). Of 1305 fresh embryo transfers, there was a significant increase in fetal heart rate per transfer from embryos in the Embryoscope (34.5% vs.27.1%,$p<0.01$). Interestingly, pronuclei was not observed during fertilisation assessment for 84 embryos that subsequently formed blastocysts cultured in the MINC, compared to only 4 embryos in the Embryoscope, suggesting that continuous monitoring increases accuracy in determining fertilisation.

Conclusion: In conclusion, embryos cultured in Embryoscope were significantly more likely to develop into a high quality usable blastocyst when compared to embryos cultured in a MINC, and importantly, this translates to a higher pregnancy rate in fresh embryo transfers.

ANZSREI Consensus Statement on Elective Oocyte Cryopreservation

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Background:
One in six Australian women and couples suffer infertility. A rising proportion relates to advanced maternal age, associated with poorer oocyte quality and IVF outcomes. Internationally, oocyte cryopreservation technology applied to oocytes vitrified before 35 years provides similar live-birth statistics compared to IVF treatment using fresh oocytes. Oocyte cryopreservation is accessible in Australasian settings and elective uptake is increasing. For women accessing treatment, oocyte cryopreservation may expand future family building options.

Aim:
To develop the first Australasian Certification in Reproductive Endocrinology and Infertility (CREI) subspecialist led consensus guideline on oocyte cryopreservation.

Method:
The ANZSREI ACCEPT (Australasian CREI Consensus Expert Panel on Trial evidence group) met in 2017 and 2018 and identified clinical aspects of care for inclusion and review. Review of the available evidence was conducted and consensus statements prepared. Areas of dissent of expert opinion and for further research were noted.

Results:
Consensus was reached on definition and best practice in oocyte cryopreservation for freeze method, controlled ovarian stimulation, medical risk reduction and treatment and outcomes counseling. The term "social egg freezing" may marginalize, stigmatize or attribute social blame to women, and there is a need to revise this to a neutral and non-judgemental term such as elective or planned oocyte cryopreservation.

Conclusion:
Oocyte cryopreservation has the potential to improve cumulative live birth outcomes for women. Implementation of this guideline should facilitate an optimal approach for providing care.

Is there a Correlation Between Scored Blastocyst and its Effect on Clinical Pregnancy Rate in Thawed Cycles?

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[1]*Department of Reproductive Medicine, KK IVF, KK Women's and Children's Hospital, Singapore*.

Background:
Our centre has moved towards performing single embryo transfers increasingly since 2016. Recently, we have been using a simplified blastocyst scoring system to grade all fresh blastocysts to assess their usability. Moving forward, we aim to review this scoring system for our thawed blastocysts in patients' frozen cycles.

Aim:
This is a preliminary study to assess if there is a correlation between the grade of the thawed blastocysts transferred and their clinical pregnancy outcomes after embryo transfers (ET).

Method:
Data of thaw cycles performed between April 2016 and September 2018 were retrospectively analysed. Cryopreserved blastocysts assessed were created by intra-cytoplasmic sperm injection and vitrified; and subsequently thawed a day before or on the day of ET, using a commercial cryopreservation kit (Irvine Scientific®). Only cycles which had single fully expanded (FE) blastocyst transferred were included (n=378, average age of patients= 34.5 years ±3.6). Frozen blastocysts which survived the thawing were rescored – either graded A, B, C or UG (ungraded). The blastocyst grade equivalent by Gardner's classification system of the inner cell mass and trophectoderm is in parentheses- A=(AA),B=(AB/BA/BB) and C=(AC/CA/BC/CB). Respective clinical pregnancy rates(CPR) and miscarriage rates(MR) were evaluated and compared. Data was then subjected to Chi-square test for analysis, with $p<0.05$ for significance.

Results:
Overall CPR/ET was 45.77%(173/378) and MR was 35.84%(62/173). Grade A or B FE blastocyst seemed to give statistically higher CPR compared to others. [FEA vs. FEB vs. FEC vs. FEUG; 69.23%(9/13) vs.64.46%(78/121) vs.32.4%(58/179) vs.43.08%(28/65); p=0.00001]. MR for ungraded blastocyst appeared to be the highest as compared to those with grades [FEA vs. FEB vs. FEC vs. FEUG; 44.44%(4/9) vs.26.92%(21/78) vs.41.38%(24/58) vs.46.43%(13/28); p=0.16, *ns*].

Conclusion:
There is a correlation between the grade of the thawed blastocysts and their outcome on clinical pregnancy and miscarriage risk after ET. A larger sample size is needed to further substantiate this.

Total	FE				
	A	B	C	UG	Total
ET done	13	121	179	65	378
Preg	9	78	58	28	173
Misc	4	21	24	13	62
CPR	69.23077	64.46281	32.40223	43.07692	45.7672
MR	44.44444	26.92308	41.37931	46.42857	35.83815
Biochem	0	8	14	5	27
Ectopic	0	1	0	0	1

Comparing between different gradings (FE)

Chi-square statistic:32.9938. p-value is <0.00001. Result: significant at p<0.05

Comparing between miscarriages

Chi-square statistic:5.1261. p-value is 0.162792. Result: not significant at p<0.05

Brief Co-Incubation Insemination vs Overnight Co-Incubation Insemination in IVF

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Background:
The in vitro fertilization (IVF) technique is commonly used in ART when the sperm quality is within the normal range. IVF involves less manipulation on both the gametes and is more cost effective. The brief co-incubation insemination protocol in IVF procedures is used as an attempt to avoid increased reactive oxygen species (ROS) produced by sperm and other products of metabolism in the co-culture system. The suboptimal culture conditions in overnight insemination protocol might cause possible detrimental effects on the oocytes and effect the fertilization and further development of the oocytes. In order to reduce the effects of ROS, the number of motile sperm for overnight insemination protocol was reduced by half the number of the brief co-incubation insemination protocol.

Aim:
Present study would like to compare the fertilization and embryos utilization rate in between brief co-incubation and the modified overnight co-incubation insemination protocol.

Method:
Insemination is carried out in 4-well Culture Dish with maximum of 6 oocytes in each well. The insemination time is approximately 39-42 hours after the HCG injection. The number of motile sperm to be inseminated each well is 200 000 sperm/mL for brief co-incubation insemination (2-3 hours) and 100 000 sperm/ml for overnight insemination. A quick check for sperm concentration is carried out under the inverted microscope equipped with heated stage to ensure that oocytes are not over or under inseminated. Insemination is then carried out at 36.5°C-37.5°C in CO_2 gas atmosphere.

Results:
Total of 445 oocytes were inseminated using the brief co-insemination protocol. Fertilization rate is 63.6% (280/445), abnormal fertilization rate is 8.3 %(37/445), embryos utilization rate is 66.1% (187/283). As for overnight co-insemination protocol, a total of 112 oocytes fertilized from 176 inseminated oocytes. Fertilization rate is 63.6%, abnormal fertilization rate is 6.3%(11/176) and embryos utilization rate is 61.6% (69/112).

Conclusion:
There are no significant different in the fertilization rate, abnormal fertilization and embryos utilization rate in both protocol ($p<0.05$). However the embryos utilization fate in the brief co-insemination protocol is slightly higher compare to the modified overnight insemination protocol. The brief co-insemination protocol is more favorable in order to produce more usable embryos. Further large prospective studies are needed to elucidate the rates of clinical pregnancy, ongoing pregnancy and rate of implantation in between these two protocol.

Effect of Paternal Age (PA) on IVF Outcome, in Association with Maternal Age (MA)

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Background:
It has been well documented that IVF outcome deteriorates with advancing MA. Lately, the role of PA on semen parameters and pregnancy outcome is being explored.

Aim:
This study was aimed to investigate the effect of PA on IVF outcome, in association with MA.

Method:
This is a retrospective review of 722 cycles (IVF/ ICSI) from 2014 to 2017. At MA<38 years old, data were grouped into category(i) PA<38 (N=300), and (ii) PA≥38 (N=189). At MA≥38 years old, data were grouped into category(iii) PA<38 (N=39), and (iv) PA≥38 (N=194). Fertilization rate (FR), embryo utilization rate (EUR), clinical pregnancy rate (CPR), miscarriage rate (MR) and live birth rate (LBR) were analyzed.

Results:
Mean MA were 33.1 and 41.2 for <38 and ≥38. Mean PA were 33.8 and 43.1 for <38 and ≥38. FR and EUR for all the groups were similar with no significant difference. At MA<38, CPR were similar for both PA groups. At MA≥38, CPR for PA≥38 was significantly lower than PA<38 (0.23vs0.45, p=0.0203). At PA<38, CPR for both MA groups showed no significant difference. However, at PA≥38, CPR for MA≥38 was significantly lower than MA<38 (0.23vs0.56, p=0.0001). At MA<38, PA ≥38 showed significantly higher MR (0.23vs0.11, p=0.019) and significantly lower LBR (0.76vs0.88, p=0.0314) than PA<38. At MA≥38, MR and LBR for both PA groups did not show any significant difference.

Conclusion:
PA and MA in combination did not show any significant effect on FR and EUR. At PA or MA<38, the partner's age did not show any significant impact on CPR. However, at advanced PA or MA, increasing partner's age lowered CPR significantly. Higher PA increased MR and lowered LBR significantly at MA<38 but showed no impact at MA≥38. CPR and LBR were the lowest and MR was the highest when both partners are advanced in age.

A Genome-Wide Association Study of Endometriosis: Data from the UK Biobank

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Background:
Increased prevalence of endometriosis among related compared to unrelated women has been demonstrated, and the heritability of the condition has been estimated at approximately 50%. Candidate genes studies have been conducted to investigate the genetic basis of endometriosis, but these have failed to produce significant results. This has led to research in the form of genome-wide association studies (GWAS) which are aimed at identifying common genetic variants that underlie a complex disorder.

Aim:
To perform a genome-wide association study in a population of European ancestry to investigate genetic factors contributing to endometriosis and to explore existing endometriosis-associated variants in the literature.

Method:
Data from the UK Biobank including 3820 endometriosis cases and 240731 controls were analysed in the GWAS using genotypes imputed from the 1000 Genomes reference panel and BOLT-LMM v2.3 software. Multivariate logistic regression analysis was performed in 12 top signals identified

Results:
One novel variant and two previously published endometriosis signals reached genome-wide significance: Chr4:55998379_TAA_T deletion (p=2.90E-08), rs11031005 (p= 1.70E-09) and rs61768001(p= 8.10E-10). A variant rs58415480 was also moderately associated with endometriosis (p= 2.90E-06). Genes related to these loci include KDR, WNT4, SYNE1, ESR1, and FSHB. Association with some previously published endometriosis SNPs was replicated.

Conclusion:
The variants identified implicate genes involved in steroidogenesis, ovarian follicular development, cell signalling pathways and maintenance of cell morphology, angiogenesis, and regulation of sex hormone levels in the development of endometriosis. Further research to assess the functional impact of these variants is required.

Preconception Carrier Screening - First 1,100 Cases

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Background:
Preconception screening has evolved from targeting specific ethnic groups. RANZCOG (2018) recommended genetic screening be offered to all prospective parents, with a basic screen for Cystic Fibrosis Spinal Muscular Atrophy and Fragile X as a minimum. Gene screening methodologies have advanced over the last decade and NextGenSequencing (NGS) is now employed by some providers, with sequencing of all coding regions of a gene and hence an increased detection rate for pathogenic/likely pathogenic variants.

Aim:
To determine carrier rates for a panel of 552 autosomal recessive genes associated with 590 genetic diseases with onset in the first 2 years of life.

Method:
Screening of 1,100 consecutive cases was undertaken with the Illumina inherited diseases panel**.** Sample origin included couples, gamete donors and donor gametes recipients. Only pathogenic/likely pathogenic variants were reported, ACMG-AMP variant interpretation guidelines were used. Data analysis included software: Illumina Variant Studio, Alamut, ClinVar, HGMD and GoldenHelix/Sentieon

Results:
Thirteen carrier couples were identified for the following genes CBS, CFTR, DHCR7, ERCC6, GALT, GJB2, PAH and TREX1. A total 637 pathogenic/likely pathogenic variants were detected, 57% in female and 43% in males. Eighteen genes had a carrier rate >1 in100: CFTR with 72 carriers (43% of these would have been missed on the Elucigene CFTR panel with 50 variants screened); GJB2 with 58 carriers, PAH with 34 carriers, CBS with 31 carriers, ATP7B with 23 carriers and POLG with 22 carriers.

Conclusion:
Carrier rates for pathogenic/likely pathogenic variants will differ between providers depending on methodology. NGS is necessary for partner screening of a known carrier for an AR disorder to excluded carrier status with greater certainty - this can never be 100%. A local database has been created for over 1,000 Australasian individuals that covers SNVs, deletions, duplications, indels, splice variants and other variants in this 552 gene panel.

Vitrification of Sperm Without Cryoprotectants: A Comparison of Two Different Vitrification Systems

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Background:
Nawroth et al (2002) showed that washed sperm could be vitrified without using cryoprotectants simply by dropping a small volume of sperm suspension directly into liquid nitrogen. This was subsequently modified to improve survival by the inclusion of non-permeable sucrose (Isachenko et al, 2008).

Aim:
To reinvestigate the vitrification using two contemporary vitrification systems of human sperm without any cryoprotectants.

Method:
After approval by the Joondalup Health Campus Ethics Committee, washed sperm preparations were made with discontinuous gradients for fresh (n=5) or frozen (n=5) normozoospermic semen samples, sperm resuspended in G-MOPS Plus (Vitrolife), and vitrified using the Rapid-iTM Vitrification system (0.3µl; Vitrolife, Sweden AB) and the Cryologic CVMTM kit (2µl; Cryologic, Australia). After warming by immersing the respective device into warm medium, sperm motility was measured immediately and after 10 mins, and a survival index (SI) calculated as (final total motility * 100 / original total motility). Comparisons between the two systems were made using paired t-test, and differences significant if $p<0.05$.

Results:
For fresh sperm after warming, the SI was 57.0 ± 2.2% and 57.2 ± 1.6% for Rapid-i™ and 54.1 ± 2.6% and 55.3 ± 2.0% for CVM kit™ at 0 and 10 minutes respectively, and was not statistically significant ($p> 0.05$). For previously frozen sperm after warming, the SI was 37.7 ± 9.1% and 36.4 ± 9.6% for Rapid-i™ and 38.8 ± 7.6% and 39.1 ± 6.2% for CVM kit™ at 0 and 10 minutes respectively. Again, there was no significant difference between vitrification systems.

Conclusion:
Sperm survival after vitrification without cryoprotectants is similar for both the Rapid-iTM Vitrification system and the Cryologic CVMTM kit. The omission of any cryoprotectant means that warmed sperm are suitable for use directly in ICSI without the need for subsequent washing, and is an advantage over systems using sucrose.

Accuracy and Precision of Four Types of Chamber Used to Measure Sperm Concentration: Results From an External Quality Assurance (EQA) Programme

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Background:
Counting chambers used to measure sperm concentration can affect accuracy and precision. However, most systematic comparisons are made by one user under experimental conditions.

Aim:
To use 11.5 years of data from an EQA programme to determine the accuracy and precision of four different types of counting chamber used under routine conditions by a large number of laboratories.

Method:
A total of 46 samples of latex beads the size of a sperm head and at a known concentration (range 1-20x10^6/ml) were sent out to participating laboratories between 2007 and 2019, one sample each quarter. Results were returned to the EQA office together with the type of chamber used, and a summary report generated containing the mean and SD for each distribution with the target concentration. Method-specific results for the latex bead samples were subsequently reviewed for haemocytometers, Makler®, Kova and Vetriplast chambers. The accuracy was judged by the bias of the distribution mean from the target concentration, and precision by calculating the coefficient of variation (=(SD*100)/mean).

Results:
There was no change in the proportion of laboratories using haemocytometers ($\chi 2$=1.56, ns), Makler® ($\chi 2$=0.01, ns) and Vetriplast chambers ($\chi 2$=0.38, ns), but a significant reduction in Kova chamber users ($\chi 2$=5.76, $p<0.05$). By 2019, 131 laboratories enrolled and 68 (51.9%) used hamocytometers, 13 (9.9%) Makler®, 29 (22.1%) Vetriplast, and 12 (9.2%) Kova chambers. For accuracy, haemocytometers < Makler®<Kova < Vetriplast (all differences $p<0.01$). Haemocytometers had a mean bias of -2.7%, Makler® counting chambers +16.9%, Kova chambers +33.2%, and Vetriplast chambers +48.9%. For precision, haemocytometers < Vetriplast=Makler® <Kova (all differences $p<0.01$). Haemocytometers had a mean CV of 14.7%, Vetriplast chambers 21.0%, Makler® counting chambers 24.4%, and Kova chambers 33.9%.

Conclusion:
Haemocytometers performed the best of the 4 chamber types confirming them to be the gold standard against which others should be compared.

Semen Analysis in African Laboratories: Is it Valid to Use the Reference Ranges from the WHO 5th Edition Manual for Clinical Interpretation?

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Background:
Semen analysis is the core screening test for male fecundity and the WHO have produced a series of manuals with recommended methodology to minimize technical variation, and reference ranges to help standardize clinical interpretation.

Aims:
To determine (a) if there is any evidence that African laboratories use WHO methods for semen analysis, and (b) whether the WHO semen analysis reference ranges are valid for African men.

Method:
ECU Worldsearch and Google Scholar were used to find journal articles. Evidence was sought to determine if racial and geographical differences exist in semen characteristics, and if African men had been included in the work undertaken by Cooper et al (2010) Hum Reprod Update 16, 231-245 to derive the reference ranges cited in the WHO 5th Edition Manual (2010).

Results:
Numerous reports show semen characteristics vary between geographical locations and racial groups (eg Andrology 1, 806; Arab J Urol 16, 3; Reprod Biomed Online 33, 684), but African men were not included by Cooper et al (2010). Surveys in Poland (Asian J Androl 15, 616), UK (Hum Reprod 20, 3441), USA (Fert Steril 78, 603) and Germany (Journal für Reproduktionsmedizin und Endokrinologie 14, 306) all showed that laboratories do not consistently use the methods recommended by the WHO to minimise technical variability. Whilst African laboratories publish data on semen quality citing the WHO 5th Edition manual (2010) as the method used, there is no evidence to show that African laboratories do use these methods widely.

Conclusion:
Racial differences exist in values obtained at semen analysis. Before the current international reference ranges published by WHO can be used, African laboratories must confirm their suitability for local African men. Standardised methods need to be used in African Laboratories before verification studies for African subjects can be undertaken.

What About Dads Age?

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Abstract:
The age of men accessing ART treatment is rising (currently 38.1 years), with over 1/3 of men aged 40 years or older (ANZARD, 2016). Given that the average age of first time fathers is rising, we need to be asking the question; Does the age of males matter in IVF success? In terms of IVF outcomes, advanced paternal age has been shown to reduce viable pregnancy rates, live birth and term birth rates, while increasing miscarriage rates independent to that of maternal age (i.e. donor oocyte cycles). Interestingly, there also seems to be an additive negative effect to pregnancy rates when maternal age is also increased. The effects to pregnancy rates due to advanced paternal age are likely due to its negative effects on semen quality altering; testicular function, reproductive hormones, sperm parameters, sperm DNA integrity, sperm telomere lengths, sperm *de novo* mutation rate, sperm chromatin structure and sperm epigenetic factors. Alarmingly, the negatively effects of advanced paternal age does not stop at pregnancy, increasing risk of a number of child disorders including neuro-cognitive (i.e. Autism), autosomal dominant (i.e. Achondroplasia), congenital abnormalities (i.e. neural tube defect) and cancers (i.e. brain). However, one of the major limitations is that there is no real consensus into the definition of advanced paternal age making counseling couples about the negative effects hard. This is because there is still debate about how age is eliciting its effects, i.e. is it due to the aging process/ or just an accumulation of lifestyle factors overtime.

What do we know About Altruistic Surrogates?

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4 Concept Fertility, Perth, Australia

Background:
In Australia there are fewer surrogates than intended parents, some of whom go overseas for commercial surrogacy because of being unable to find a surrogate. Increased knowledge of the characteristics of surrogates would be helpful for intended parents in locating a surrogate and for clinics in optimizing psychosocial support of surrogates.

Aim:
Prior research in the USA investigated psychological characteristics of gestational carriers, but no studies have characterized altruistic surrogates. The current study aimed to comprehensively assess the socio-demographic and psychological characteristics of altruistic surrogates.

Method:
Recruitment was from a clinical practice over 15 years and part of a larger cross-sectional study. N = 160 surrogates seen for pre-surrogacy assessment counselling at a Sydney-based independent psychology practice. Main outcome measures: responses to a pre-surrogacy counselling protocol including socio-demographics and responses to the Personality Assessment Inventory (PAI).

Results:
Surrogates (124 partnered, 36 single) with a mean age of 37.4 years, were primarily sisters or sisters-in-law (48.6%), or a friend or extended family member of an intended parent (46.3%). A small percentage (5.1%) of surrogates was recruited from internet forum support groups. Surrogates are most likely to have completed education to Year 10 (32.1%), have a semi-professional occupation (31.9 %), and live in a high socio-demographic post code area (34.4%). There was no significant PAI psychopathology found though there were significantly lower Grandiosity (49.11) and Social Detachment (44.68) subscales, and elevated Interpersonal Warmth (55.68). Qualitative analysis indicated values of: surrogacy is “special”, empathy, sisterhood, good at pregnancy, importance of parenting, and importance of relationships.

Conclusion:
The findings will aid intended parents to look for a surrogate, and indicate the importance of family and informal networks. Sociodemographic and PAI findings are also helpful in surrogacy counselling.

Fragile X, handle with care: ethical implications of preconception carrier screening

Di MILNES

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Abstract:
Population-based reproductive carrier screening for heritable genetic conditions is rising in prominence. The future landscape of genetic testing in Australia may one day see universal publicly funded reproductive carrier screening, the goal of Rachael and Jonny Casella, the face of Mackenzie's Mission. But the routinisation of screening does not obviate the need for informed financial consent. The pre-test counselling session must provide the couple with information about their risk of being a carrier, the clinical pathways for utilising the information screening provides, limitations of the screening test and a supported environment in which to explore whether this information is desirable in the context of their personal values and reproductive goals. Preserving autonomy in decision making both in consenting to the screening test and to any interventions that may follow is key to ensuring no harm is done in the integration of population-based preconception carrier screening into reproductive medicine in Australia. A case study in Fragile X syndrome will illustrate the importance of pre-test counselling in carrier screening.

Internet of Things: Coming to an ART Laboratory Near You

Dean MORBECK

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Background:
Internet ready devices surround us both personally and at work, devices which connect in the cloud to make the Internet of Things (IoT). In our everyday lives, these include mobile phones, coffee makers, washing machines, headphones, lamps, wearable devices and almost anything else you can think of. This also applies to components of machines, for example a jet engine of an airplane or the drill of an oil rig. If the device has an on an off switch, then chances are it can be a part of the IoT. People, too, can be connected to the IoT, establishing people-people, people-things, and things-things relationships. The IVF laboratory is perfectly suited for IoT monitoring and, coupled with artificial intelligence, provides a layer of information that will likely revolutionize how we work.

PIEZO ICSI with Spindle Confirmation (New Era of Ultimate ICSI Approach)

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Background & Aim:
First successful ICSI was reported in 1992, however, basic concept and approach has not been changed. During those more than 25 years, ART Labo technology has been dramatically improved along with scientific achievement and technological development Why not to think something better in ICSI? In this presentation, how PIEZO ICSI(p-ICSI) could improve the strategy of ICSI and ART results will be introduced,

Method:
As you know, conventional ICSI(c-ICSI) requires bevel thin narrow pipette with sharp spike and either aspiration of cytoplasm or twisting pipette in order to puncture the plasma membrane of oocyte, Technical performance of ICSI depends on the elasticity of membrane and skill/experience of embryologists. However,p-ICSI only needs one single PIEZO pulse that create ultrafast submicron forward momentum with thin flat-tipped pipette to break the plasma membrane and to introduce the sperm into inside the egg. Also multiple PIEZO pulse creates a hole of zona pellucida(ZP) without any deformity of ZP. Since Aug, 2017 in our program, ICSI method was changed c-ICSI to p-ICSI completely to improve the fertilization rate and to decrease degeneration rate.

Results:
In 2013-14, c-ICSI was carried out on 3522 oocytes in 587 cycles(Ave age;38.6) and in 2017-18, p-ICSI on 5892 oocytes in 870 cycles(Ave.age;39.3). Fertilization rate and degeneration rate of c-ICSI and p-ICSI were 66.8%vs76.7% and 9.3% vs 3.8%, respectively. Blastocyst development rate were c-ICSI(41.9%) and p-ICSI(52.7%).

Conclusion:
Since p-ICSI to all cases was introduced in 2016, fertilization, degeneration and blastocysts development rate has been improved statistically($p<0,001$), comparing with c-ICSI. This could create more number of embryos available and indicate p-ICSI would be less invasive approach than current ICSI because of improvement of blastocyst rates.

Fresh Versus Frozen Surgical Sperm Retrieval for IVF-ICSI

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Background:
The adage “fresh is best” is often employed, however there is controversy in the literature with regards to the use of fresh versus frozen surgical sperm retrieval (SSR) in Intracytoplasmic Sperm Injection (ICSI) In Vitro Fertilisation (IVF) treatment.

Aim:
To determine if the use of frozen SSR for ICSI gives comparable live birth rate, clinical pregnancy ratesand miscarriage rate to the use of fresh SSR. In addition, the analysis compares female and male age at the time of the procedure, cause of azoospermia (non-obstructive versus obstructive) and fertilisation rates.

Method:
A retrospective analysis was performed of all IVF-ICSI pregnancies over a 14 year period at two IVF providers in New Zealand using a clinical database. Relevant descriptive statistics were extracted and determined. Statistical analysis using Fisher-Exact and multi-variable Binary Logistic Regression were performed.

Results:
The first live birth per couple was analysed, therefore 1093 Oocyte Pick Up (OPU) cycles were included (948 frozen SSR and 145 fresh SSR) from 1 January 2002 to 31 December 2015 from two clinics. Of the total OPU cycles, 64% had a documented cause of the azospermia.

The two groups were comparable as there was no statistically significant difference in the mean age at the time of procedure ($p = 0.65$), fertilisation rates ($p = 0.46$) and miscarriage rates ($p = 0.99$).

The Fisher-Exact analysis showed there was a higher live birth rate ($p = 0.016$) and clinical pregnancy rate ($p = 0.013$) with frozen SSR versus fresh SSR and this was statistically significant. We do not believe this is clinically significant due to regional selection bias between the two groups and lower numbers in the fresh SSR group.

Furthermore, the multi-variable analysis confirmed the bias by showing when controlling for clinic, type of azospermia, female age, male age and fertility rate; the type of sperm (fresh versus frozen) does not have significant effect on having a live birth (OR 0.754 (0.427, 1.335), $p = 0.33$) or a clinical pregnancy (OR 0.787 (0.452, 1.367), $p = 0.59$).

Analysis of obstructive versus non-obstructive azospermia showed there was no statistically significant difference in live birth rate for fresh SSR ($p = 0.89$) versus frozen SSR ($p = 0.55$) or clinical pregnancy rate for fresh SSR ($p = 0.85$) versus frozen SSR ($p = 0.28$).

Conclusion:
In summary, the retrospective analysis demonstrates that the use of frozen SSR gives satisfactory and comparable live birth and clinical pregnancy rates in ICSI and this remains consistent despite the underlying cause for azoospermia.

Estimating the Need for Assisted Reproductive Technology in Australia

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Background:
10-15% of couples attempting pregnancy fail to conceive within one year and are classified as infertile. Assisted reproductive technology (ART), specifically in-vitro fertilization and intracytoplasmic sperm injection, is an increasingly common method of treating infertility despite its relatively stable and comparable prevalence across developed nations. Government subsidies and commercial interests drive ART expansion, leading to potential unnecessary use over alternatives such as expectant management and intrauterine insemination (IUI) which can achieve similar cumulative live birth rates in a significant proportion of cases. ART represents a costly, invasive procedure which carries numerous maternal and perinatal complications, hence quantifying the proportion of couples absolutely requiring ART to achieve live birth may help reduce unnecessary use.

Aim:
To determine Australia's maximal annual demand for infertility treatment with ART.

Method:
We estimated the number of infertile couples within Australia in 2015 using the number of non-ART births, stillbirths, miscarriage rates and population infertility rate. Couples were categorized by infertility causes into absolute ART indications (tubal blockage, severe sperm factor) or indications initially treatable with IUI, ovulation induction or expectant management provided good natural fertility prospects. A decision-tree was used to determine treatment with either expectant management, IUI, ovulation induction or direct to ART, resulting in an estimate the need for ART procedures.

Results:
We estimated the number of couples attempting pregnancy in Australia in 2015 who failed to conceive spontaneously to be 60248. The estimated number of infertile couples requiring ART in these couples was calculated to be 40658, which is marginally higher than the 36162 women who received ART in 2016. The number of couples first treated with expectant management, IUI and ovulation induction was 16252, 22544 and 12050, respectively.

Conclusion:
An overestimation for calculated ART demand based on infertility prevalence approximates the actual volume of ART use in Australia, suggesting potential ART over-utilisation.

Apodized Phase Contrast Microscopy Reveals Fine Granules and Fibrous Structures in Early Embryos

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Background:
No microscopy staining methods are applicable clinically in assisted reproductive technologies. To this end, we developed apodized phase-contrast microscopy to reduce halo artifacts when imaging fine anatomical structures. This technology uses an apodized phase plate at the Fourier transform plane in the objective lens, which both weakens the diffracted light produced by large objects to lower their relative image contrast and increases the contrast of small objects. We previously visualized unstained fine granules and fibrous structures in early mouse embryos by apodized phase-contrast microscopy.

Aim:
The purpose of this study is to reveal structures and differences in human embryos and oocytes, especially fine granules in perivitelline space and inner granularity. We subsequently used this new type of microscopy to analyze human embryos and oocytes.

Method:
Apodized phase-contrast microscopy was performed using an inverted microscope and a stage-top incubation system (Tokai Hit). A plan fluor objective lens with magnification 40X, NA 0.75 (CFI Plan Fluor 40X, developed ABH contrast, Nikon) and a digital camera (Ds-Ri2, Nikon) were used with specific wavelength filters (Edmund Optics Japan). Time-lapse imaging was performed at high speed (e.g. 1 frame/s).

Results:
By apodized phase-contrast microscopy, we observed fibrous structures in mouse and human embryos and oocytes, as well as fine granules in the perivitelline space. Fine granules in the perivitelline space were observed in some human embryos. The granularity was observed not as granular structures but as fibrous structures with high contrast than surrounding area.

Conclusion:
Fine granules and fibrous structures in human and mouse embryos were observed, including fine granules in the perivitelline space. Areas of granularity were observed as fibrous structures with high contrast that showed different refractive index dispersion from that in the surrounding area. We showed that this microscopy improves the visualization of human embryos and oocyte for clinical use.

What About the Age of the Blastocyst: Day 4, 5, 6 or 7?

Dr Leanne PACELLA-INCE[1,2]

[1]*Repromed, Adelaide and Darwin, Australia,* [2]*Fertiltiy Tasmania, Hobart, Australia,*

Abstract:
Assisted reproductive technology (ART) is no longer experimental science and is now considered standard medical treatment. During the evolution of ART, our understanding of embryo physiology has led to significant improvements in the laboratory in regards to the technology (culture media design, gas phase, fertilisation techniques, and cryoperservation methods) such that pregnancy rates have significantly improved. These improvements have led to a significant increase in extended embryo culture with blastocyst transfer becoming routine practice in IVF clinics to increase subsequent pregnancy rates.

Studies have demonstrated that extended culture and transfer (day 4 or 5) results in significantly increased pregnancy rates compared to cleavage stage transfer (likely due to increased selection pressure on the embryo cohort as well as transfer of the embryo into the uterus at the correct time). The culture beyond day 5 is also routine practice however whether transfer at these later stages is a viable alternative is a matter of debate. Evidence suggests that embryo transfers on day 6 can result in a reduction in implantation rates and the embryo should be frozen and transferred in a subsequent frozen embryo transfer cycle where pregnancy rates between day 5 and 6 are similar. As human blastocysts initiate implantation by day 8, it also seems reasonable to culture embryos to day 7 if required however the circumstances that dictate this should be based on patient need, including the requirement for an expanded blastocyst to be genetically tested. Whether day 7 culture should become routine practice remains controversial.

Where to Now for Surrogacy?

Stephen PAGE[1]

[1] *Page Provan, Brisbane, Australia,*

Background:
Surrogacy law and practice in Australia has continued to remain in a state of flux. There have been surrogacy or surrogacy/ART reviews federally, and in NSW, South Australia, Victoria and Western Australia.

At the time of writing, there is pending legislation in both South Australia and Western Australia concerning surrogacy.

The Northern Territory is now considering enacting laws concerning surrogacy.

Australians continue to undertake surrogacy overseas. This poses challenges for Australian policy makers, due to concerns about commercial surrogacy. There are four jurisdictions in the world that criminalise overseas commercial surrogacy. Three of those are in Australia. It has been recommended in an inquiry that a fourth Australian jurisdiction, Western Australia, specifically criminalise overseas commercial surrogacy journeys- an approach rejected in a similar review in South Australia as unworkable.

In five Family Court cases, judges registered or refused to register US surrogacy orders, based primarily on their views about what was commercial surrogacy. Two of those cases have given clarity in both Queensland and NSW about what is and what is not commercial surrogacy.

The reserved decision of the High Court in Masson v Parsons – in which Mr Masson sought to become a father, but was held by a lower court not to be one- is likely to impact on donation and parenting issues, whichever way the High Court may decide.

The Western Australian case of Piccolo and Piccolo concerned the ability to use an embryo following the separation of a couple- in circumstances when the husband wanted to become a parent again, possibly through surrogacy in Canada.

The Hague Conference on Private International Law continues to move towards a convention covering overseas surrogacy journeys. The Hague working group of experts has proposed a model based on comity of judgments recognising intended parents as the parents of child born through surrogacy.

The United Nations Special Rapporteur on the Sale and Sexual Abuse of Children, and the Use of Children in Pornography has called many current international surrogacy practices, such as binding contracts and pre-birth orders tantamount to the sale of children. The Special Rapporteur is calling for a public international law response to surrogacy.

Aim:
The aim is to educate attendees about the current state of the reviews, an update of the law across Australia, and international trends- including where Australians undertake surrogacy journeys, and the approaches and likely impact of both The Hague and the Special Rapporteur's actions.

Method:
By setting out the law, including caselaw, review recommendations and overviews, and overview of the processes with The Hague and the Special Rapporteur. This comes from my unique legal practice (in which I was on the record for four of the five registration cases) , as well as from my involvement in submissions to the Federal, NSW, Victorian, South Australian and Western Australian reviews, and through my being a member of the International Academy of Family Lawyers parentage/surrogacy committee, as well as being an international representative on the ART Committee of the American Bar Association (and from that role having a watching brief on international developments, including being co-author of that Associations' Hague surrogacy policy-

which policy is largely adopted in the current report of the Hague working group of experts as the model for a convention).

Results:
As above.

Conclusion:
Surrogacy law and practice remains in a great state of flux, both across Australia and internationally. Those attending will become aware of both local and international developments.

Comparing Pregnancy Outcomes Between Natural Cycles and Artificial Cycles Following Frozen-Thaw Embryo Transfers

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Background:
With respect to endometrial preparation in frozen-thawed embryo transfers (FET), artificial cycle (AC) preparation is often adopted over the natural-cycle (NC) for practical purposes, to facilitate access to FET. However, there is current a paucity of evidence comparing pregnancy outcomes between these two commonly-used cycle types.

Aim:
To compare pregnancy outcomes between NC and AC, including biochemical, clinical and live birth rates, as well as miscarriage rate with particular regard to the progression to live birth from first biochemical diagnosis of pregnancy.

Method:
This is a large single-centre retrospective analysis, examining a standardized data set from 2015-2018. This comprised N= 3165 cycles (NC, N=2111, AC, N= 1054). The main outcomes of interest were biochemical pregnancy (beta-hCG $\geq$5), ultrasound-diagnosed clinical pregnancy, and live births. Using the chi-squared test, the above pregnancy outcomes were compared between NC and AC. A multivariate logistic regression, controlling for factors such as age, embryo quality, and day of blastocyst freeze was further utilised to assess for confounding variables.

Results:
Whilst no difference was observed between biochemical pregnancy rates for the two cycle types (NC vs. AC, 38.37% vs. 37.00%, P = 0.455), statistically significant differences were observed with respect to clinical pregnancy (29.65% vs. 25.33%, P = 0.011), and live birth rates (18.43% and 13.28% P = 0.000). Additionally, a multivariate logistic regression was performed, demonstrating that NC produces superior pregnancy outcomes when controlling for the afore-mentioned factors.

Conclusion:
This study demonstrates superior continuing pregnancy rates following NC when compared to AC, with high rates of miscarriage, and consequently, lower live birth rates in AC. These findings suggest that NC should be be the cycle of choice, when possible, and highlight the need for randomized control trials to further evaluate this question.

Progesterone Levels on Day of Embryo Transfer Do Not Predict Pregnancy Outcomes in Artificial Frozen-Thaw Cycles.

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Background:
Progesterone (P4) is vital for endometrial preparation prior to frozen-thawed embryo transfer (FET). Although the significance of P4 levels during the late-follicular and luteal stages has been well studied, current understanding of optimal P4 ranges at embryo transfer is still limited.

Aim:
To investigate whether P4 levels on day of artificial FET correlate with pregnancy outcomes.

Method:
This is a large single-centre retrospective cohort analysis of a standardised data set spanning 2015-2018. This comprised of N=2010 FETs into hormonally prepared endometria. In these cycles, P4 levels prior to embryo transfer were assessed in relation to biochemical pregnancy (beta-hCG≥5), ultrasound diagnosed clinical pregnancy, and live birth rates. Similar to previous studies in the area, a P4 threshold of 10ng/mL (31.8nmol/L) was used to simulate the currently accepted level for physiological corpus luteal function. A total of 807 FETs were completed in patients with P4 levels below 10ng/mL and 1203 FETs in patients with P4 levels at or above 10ng/mL. Using the Chi squared test, pregnancy outcomes were compared between these two cohorts. A multivariate logistic regression, controlling for factors such as age and embryo quality, was further used to assess the relationship between P4 levels and outcomes.

Results:
We observed no statistically significant difference in pregnancy outcomes between the two cohorts (P4 on FET day <10ng/mL versus >/=10ng/mL). This was uniformly demonstrated across biochemical pregnancy rates (39.53% vs. 40.98%, p=0.516), clinical pregnancy rates (20.82 vs. 22.78, p=0.299) and live birth rates (14.25 vs. 16.21 p=0.233). Additionally, multivariate logistic regression also failed to demonstrate statistically significant differences in biochemical pregnancy, clinical pregnancy and live birth rates.

Conclusion:
Contrary to previous studies, we demonstrated that P4 levels at or above 10ng/mL on day of artificial FET are not associated with statistically significant improvements in biochemical pregnancy, clinical pregnancy or live birth rates.

The Emotional Impact of Miscarriage & The Support Required

Samantha PAYNE[1]

[1] *The Pink Elephants Support Network - Co Founder & Managing Director*

Background:
1 in 3 women will experience a miscarriage in Australia, 283 couples a day report an early pregnancy loss. Global research has demonstrated that miscarriage is associated with significant distress, grief and loss, and in some cases clinically significant levels of depression and/or anxiety. Despite these consequences for women's emotional and mental health, studies have commonly found that women feel that healthcare providers often lack empathy, support, and acknowledgement of their loss.

Aim:
The aim of this presentation is to explore the emotional impact of early pregnancy loss and the ongoing emotional support that should be offered.

Method:
The Pink Elephants Support Network have ran numerous surveys from focus groups, to online surveys examining over 2000 women's experience of miscarriage support after experiencing an early pregnancy loss.

Results:
It has been found that significant numbers of women feel unsupported after experiencing an early pregnancy loss. 75% we surveyed felt unsupported through early pregnancy loss only 22% received a referral for any support post their loss. The majority of women surveyed expressed their dismay at receiving no support and would have liked more emotional support.

Conclusion:
A number of recommendations are being made the strongest being ensuring a woman and her partner are referred to a support organisation after the diagnosis of an early pregnancy loss that can offer them emotional support.

The Development of an Innovative Psychoeducational Program to Support Patients Embarking on Assisted Reproductive Treatment (ART).

Suellen PEAK
[1]*The ART Space , Melbourne, Australia,*

Background:
The transition into Assisted Reproductive Treatment (ART) can be an unwelcome and challenging step for many patients. While the Victorian context mandates counselling prior to the commencement of ART, many patients start treatment without information that can support their psychological and emotional adjustment. Psychoeducation (PE) is a systematic, structured, and didactic intervention that integrates emotional and motivational aspects. Research suggests that PE is process that supports patients to deepen their understanding of their diagnosis and offers insights into ways that patients can maintain their own emotional health and wellbeing.

Aim:
To develop a psychoeducation program to support patients commencing ART to better understand and prepare for the treatment journey.

Method:
Research studies and counselling recommendations from the NHMRC guidelines, ANZICA and the Victorian ART Act were reviewed. Managing expectations, transfer of information, skills development, and training in self help and coping emerged as key themes for inclusion in the program.

Results:
A 10 week psychoeducational program comprising 5 modules has been developed. The program delivery includes interactive webinars, written educational information and self-directed learning, with follow up coaching support.

Conclusion:
Psychoeducation is among the most effective of the evidence-based practices that have emerged in both clinical trials and community settings. Because of the flexibility of the model, which incorporates both illness-specific information and tools for managing related circumstances, psychoeducation has broad potential for many forms of illnesses and patients experiencing a variety of life challenges. Fertility patients and those navigating infertility treatment are no exception. Endurance to treatment and improved wellbeing are anticipated outcomes of this program.

Supporting Wellbeing After Early Pregnancy Loss – How Positive Psychology Can Support Resilient Grieving.

Suellen PEAK
The ART Space

Background:
Miscarriage is not a rare phenomenon in Australia. Despite 1 in 4 pregnancies ending in miscarriage it remains a topic that is rarely discussed in public. The experience of miscarriage is unique to each individual, however for infertile women, the grief experience can be interrupted through a need to commence treatment if they wish to pursue their dream of having a family.

Aim:
Drawing on psychological concepts from the field of positive psychology and bereavement research, this presentation explores practical strategies to support clinicians, ART services and patients to be active participants in grief after pregnancy loss.

Method:
A **Resilient Grieving Model** to support wellbeing is advanced. This model differs to stage theories of grief by offering agency to the bereaved, helping patients to identify their own strengths, needs and actions to navigate the grieving process. The role of helping professions is examined and options to support patients to grieve are offered.

Results:
The model recognises that grief is an inherent aspect of wellbeing and considers a variety of interventions that offer a place for grief to flow. By supporting patients to be active participants in their grief, patients may experience a wellbeing advantage in undertaking subsequent fertility cycles.

Conclusion:
Positive psychology interventions offer an active way for patients to reach out, talk, connect and share their experiences of early pregnancy loss. Resilient grieving offers an invitation to patients and professionals to lean in with intensive care, compassion and courage to challenge the prevailing experience of secrecy and to honour what has been loved and lost.

The Couples Journey Through Infertility

Brennan PETERSON[1]

[1]*Chapman University, USA*

Abstract:
Couples experiencing infertility are faced with a multitude of stressors and unexpected difficulties. Changes in social, family, and relationship dynamics add an unexpected burden in addition to the stress of fertility treatments. While some couples grow closer because of the infertility experience, the stressor of infertility can erode the strength and stability of even the most satisfied relationship. Fortunately, health care professionals can provide support that can assist couples in the challenges they face. The presentation will highlight the challenge of couples experiencing infertility. Gender differences in how couples communicate and cope with infertility distress will also be discussed. Additionally, it will explore the impact of infertility on a couple's sexual relationship, strategies to help couples best share infertility-related treatment information with others, providing guidance related to future treatment decisions, and the importance of working through grief and loss. Lastly, the presentation will examine the implications for health care professionals as they seek to provide support to the couples they treat.

The Male Perspective of Patient Care and Fertility Counseling

Brennan PETERSON[1]

[1]*Chapman University, USA*

Abstract:
Although female factors have historically been viewed as the primary cause of infertility, only one third of cases are directly attributable to women. An additional one-third of infertility diagnoses are attributable to directly to men, and another one-third are a combination of both male and female factors. Because studies examining the impact of infertility have traditionally focused on women, men's reports of their infertility journeys have been underrepresented and are often misunderstood. While many have believed that men are not emotionally impacted by infertility, recent studies show that men actually experience a variety of complex emotional reactions to an infertility diagnosis. Feelings of failure, helplessness, and threats to their perceptions of masculinity are common. Men also experience grief associated with confronting unfulfilled expectations related to not having their own biological child to mentor, teach, and pass on generational traditions. In addition, men commonly report feelings they have little to contribute to medical treatments – even in cases of male-factor infertility. This presentation will highlight what we know about men's experience of the infertility journey and will discuss strategies for health care providers to best involve men in the treatment process.

Long-Term Adjustment After ART Treatment

Brennan PETERSON[1]

[1]*Chapman University, USA*

Abstract:
Becoming a parent is one of the most universal goals of men and women throughout the world. As such, biological parenthood represents a normative and expected life-cycle transitions they plan to experience. Infertility, however, blocks the attainment of this assumed reality, and as such, represents a significant developmental interruption in their expected life course. In this regard, infertility can be perceived as a failed life course transition, or a 'transition to non-parenthood.' While ART can provide a pathway to parenthood for many couples, not all couples who undergo ART will achieve biological parenthood. This presentation will examine the long-term psychosocial implications of patients who underwent successful and unsuccessful ART treatment. Implications for health care professionals will be discussed for both groups of patients.

Are Influences of Temperature and pH Truly Separable

Thomas B POOL[1]

[1]*Fertility Center of San Antonio, San Antonio, Texas USA*

Abstract:
It is commonly accepted that a stable temperature of 37°C is crucial to the maintenance of normal spindle dynamics in the human oocyte and that even slight, transient perturbations can cause irreparable damage. This concept is based largely on data from very small numbers of oocytes obtained indirectly for experimentation or under conditions where insufficient time for repolymerization was allowed. Nonetheless, reduced temperature is invariably assigned culprit status as a direct hindrance to normal spindle dynamics. An equally plausible interpretation is that temperature fluctuations are affecting other processes and the question arises does this involve pH in some way? The use of bicarbonate buffer in oocyte and embryo culture relies upon the dissociation of carbonic acid into hydrogen ion and bicarbonate ion. Since carbonic acid is a weak acid, it follows the law of mass action as a reversible reaction and the acid dissociation constant characterizes it. This constant is clearly influenced by temperature, meaning that pH alterations may well influence spindle behavior. Recent elegant experiments in an animal model from an Australian group now confirm this reality using non-invasive measures of spindle retardation, blurring the mechanistic lines between temperature effects upon tubulin polymerization directly and via pH.

The Marriage of IVF and Cryobiology – A Brief History of the Wedding

Thomas B POOL[1]

[1]*Fertility Center of San Antonio, San Antonio, Texas USA*

Abstract:
It was the summer of 1972, in the Oak Ridge, Tennessee laboratory of cryobiologist Peter Mazur, where he, along with Stanley Leibo and visiting scientist David Whittingham, raised beakers filled with champagne in a toast to the birth of a mouse. But it was no ordinary mouse; it, in fact was the first mammal born from the transfer of a frozen embryo. Thus, the first member of the wedding party came on the scene. The other was obviously the successful collaboration of Steptoe and Edwards in Oldham exemplified by the birth of Louise brown in 1978. But it was work in Australia that produced the wedding. In modern day training, young clinicians and embryologists rarely have the time to master their respective crafts, let alone trace the historical events that have produced the contemporary amalgamation of human IVF and cryobiology. There is, however, an instructive path to follow, from Edinburg to Cambridge with a detour through Mill Hill in the UK that chronicles some details of the wedding party that should be of interest to all in reproductive medicine.

Human Oocytes and Embryos – The Myth of Temperature

Thomas B POOL[1]

[1]*Fertility Center of San Antonio, San Antonio, Texas USA*

Abstract:
One of the hallmarks of good quality management in the clinical IVF laboratory is the assurance that temperature as close to 37°C as possible is maintained in the environment of human oocytes and embryos from retrieval until transfer or cryopreservation. Declarations in the literature proclaim the deleterious or lethal effects of deviations cooler than this but do so without direct experimental evidence from high quality material, maintained appropriately for experimentation and in meaningful numbers. The evidence offered for exquisite temperature sensitivity is mostly derived from material subjected to subpar conditions prior to experimentation, to material already used for clinical IVF and thus aged or in trials with small numbers where insufficient time for recovery to temperature excursions was not allowed. Our experience with nonhuman primate oocytes and embryos, obtained with work conducted over three decades ago, indicated these conclusions were inaccurate. We have since extrapolated handling procedures developed for that model to human material and have proof, with thousands of healthy human oocytes, that our universal beliefs regarding temperature sensitivity are inaccurate.

Differences in 2-Cell and 4-Cell Embryo Quality in Relation to Sperm Developmental Status as Assessed by Time-lapse Technology

Georges RAAD[1], Cosette NADER[1], Jessica AZOURY[1], Joan AZOURY[1], Joseph AZOURY[1] and **Hassan W. BAKOS** [2]

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[2]*Monash IVF Group, Sydney, NSW, Australia*

Background:
Until recently in human embryos, the first cleavage divisions were thought to be controlled exclusively by maternal factors. However, the effect of epididymal or testicular extracted spermatozoa on early embryo development is still a matter of debate.

Aim:
The aim of this study was to assess the relationship between the sperm developmental status with the 2-cell and 4-cell embryo quality.

Method:
A retrospective study was conducted at Azoury IVF clinic. It included 86 infertile couples, where the female partners were less than 38 years of age, at the time of intracytoplasmic sperm injection. The selected couples were divided into four groups: ejaculate normozoospermia group (n=23 couples, n=133 embryos); ejaculate oligozoospermia group (n= 22 couples, n= 109 embryos); percutaneous epididymal sperm aspiration (PESA) group (n= 21 couples, n=119 embryos), and testicular sperm aspiration (TESA) group (n= 23 couples, n= 123 embryos). Only data from embryos with normal fertilization cultured in the Embryoscope were included in this study.

Results:
At the 2-cell embryo stage, a statistically significant higher percentage of embryos with unevenly sized blastomeres in the TESA group (58.4%) compared with the normozoospermia (26.3%, $p<0.001$) and oligozoospermia (42.57%, $p<0.05$) groups was found. In addition, there was a statistically significant lower percentage of 2-cell embryos without multi-nucleation in the TESA group (27.92%) compared with the normozoospermia (64.46%, $p<0.001$) and opligozoospermia (40.59%, $p<0.05$) groups. Furthermore, at the 4-cell stage embryo, the percentage of tetrahydral-shaped embryos was significantly lower in oligozoospermia (32.35%, $p<0.001$), PESA (32.14%, $p<0.001$) and TESA (27.04%, $p<0.001$) groups compared with normozoospermia group (59.04%).

Conclusion:
To our knowledge, this is the first report providing evidence that early embryo developmental competence is influenced by the sperm source as assessed by the EmbryoScope. The flow on effect from these findings should be investigated in appropriately designed randomised controlled trials to further inform the clinical practice of surgically retrieved sperm.

The Sequential Embryo Transfer Compared to Blastocyst Embryo Transfer in IVF Cycle.

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[1] *Tehran University of Medical and Science, Tehran, Iran*
[2] *Tehran University of Medical and Science, Moonee Ponds, Victoria*

Background: Repeated implantation failure (RIF) is determined when the transferred embryos failed to implantation in at least three-repeated in vitro fertilization (IVF) with 1–2 of high- quality embryos in each cycle

Aim: The purpose of this study was to determine the pregnancy rate in the double sequential transfer of embryos on day 2 and on day 5 compared to day 5 alone, in IVF/ET in patients with the three repeated consecutive IVF failures.

Method: In this controlled trial, Women scheduled for IVF/ET with the three repeated consecutive IVF failures were randomized to either sequential transfer of embryos on day 2 and on day 5 after ovum pick-up (Group I,n =60) or blastocyst embryo transfer on day 5 (Group II,n =60) as a control group.

Results: primary outcome measures were the chemical and clinical pregnancy rate.
Baseline and cycle characteristics were comparable in both groups. Clinical pregnancy rate was similar in the sequential ET group (40%) compared to the day 5 of embryo transfer group (38.3%) (P value =0.85).

Conclusion: It seems that the double embryo transfer does not increase the chance of pregnancy rate compared to blastocyst embryo transfer on day 5 in the patients with the three-repeated IVF–embryo transfer failure

Fertility Preservation in Oncology Patients: Access to Oncofertility Services in Australia for Adolescents and Young Adults

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Background:
In Australia, between the years 2010 and 2014, over 4500 adolescents and young adults (AYAs) (15–25y.o) were diagnosed with cancer.(1) Mortality rates for AYAs have decreased by 1.9% per year,(3) and survival rates are quoted as high as 78% in Australia.(2–5) Oncofertility is an emerging discipline that seeks to preserve and restore the reproductive future of cancer patients.

Aim: To examine current literature on the access to and uptake of fertility preservation in AYA oncology patients in Australia.

Method: A systematic approach according to PRISMA guidelines was applied. Databases included Medline, Cochrane Review, SCOPUS and CINHAL. A quality assessment of publications and national guidelines was completed from January 2008 to July 2018.

Results:
There is a paucity of Australian data on oncofertility. No randomized controlled trials were included in the Australian cohort; the majority of Australian research were case studies, review articles and a focus on the oncofertility, 'FUTURE' database.(6) COSA has distributed guidelines to clinicians outlining a summary of recommendations in managing AYAs fertility preservation.(7) These include an early discussion of future fertility and preservation options, providing clear and comprehensive information, use of multi-disciplinary team, development of protocols and pathways to ensure an adequate service is provided and psychological support

Barriers to accessing fertility services within Australia include a lack of clear referral pathways, financial restrictions and access to resources, education and training. Additionally, lack of long-term data can inhibit the ability to provide fertility preservation to AYAs. Both clinicians and patients have identified that this lack of data on long term outcomes, risks and side effects to patients prevented uptake of services provided.

Conclusion: With increasing rates of cancer diagnoses, it is imperative that oncofertility services become easily accessible to all patients and increased awareness should be promoted within the medical community. A multi-disciplinary approach with collaborative communication with oncologists is key to providing this service within Australia.

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Fertility Preservation in Adolescent and Young Adult Oncology Patients

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Background:
In Australia, between the years 2010 and 2014, over 4500 adolescents and young adults (AYAs) (15–25y.o) were diagnosed with cancer.(1) Mortality rates for AYAs have decreased by 1.9% per year,(3) and survival rates are quoted as high as 78% in Australia depending on type of malignancy.(2–5) The ability to reproduce and an individual's fertility is a commonly studied quality of life measure,(6) and with many of these patients living well into and beyond their reproductive years, the emergence of oncofertility and the importance of fertility preservation has become paramount.

Aim:
To examine current practice of fertility preservation in AYAs.

Method:
A systematic approach according to PRISMA guidelines was applied. Databases included Medline, Cochrane Review, SCOPUS and CINHAL. A quality assessment of publications and national guidelines was completed from January 2008 to July 2018.

Results:
Cryopreservation of both oocytes and embryos remains the gold standard recommendation for fertility preservation. In Australia, up to 90% of oocytes and embryos will survive the freeze/thaw process.(7-9) The use of GnRH analogues to suppress ovarian function is becoming increasingly more common and has been utilized in women with breast cancer, haematological and other malignancies. Pre-pubescent patients can be offered ovarian transposition and ovarian tissue cryopreservation. Ovarian tissue cryopreservation is experimental and entails surgical removal of ovarian tissue that is cryopreserved and can later be re-implanted or used in vitro for maturation and follicular development.

Sperm cryopreservation is first line management for fertility in post pubescent oncology patients. It is safe, reliable and has been utilized for decades. Other options include testicular sperm extraction and shielding of the testes both mechanically and chemically. Research into testicular tissue cryopreservation for spermatogonia stem cell transplantation has shown promising results with up to 95% viability in post thawed tissue.(10)

Conclusion: Oncofertility is an emerging discipline that seeks to provide safe, efficient and effective fertility preservation options for AYAs diagnosed with cancer. There are several fertility preservation options for patients, further research into options for pre-pubescent patients is warranted.

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Comparison of Two Anti-Müllerian Hormone Automated Assays and Suitabilty for a Companion Diagnostic for Individualised Gonadotrophin Dosing.

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Background:
Anti-Müllerian hormone (AMH) has been identified as one of the best tools for individualised gonadotrophin dosing. AMH, along with body weight, has allowed for the development of the first dosing algorithm for tailoring treatment with follitropin delta.

Aim:
To determine if anti-Müllerian hormone (AMH) automated immunoassays (Roche, Elecsys® AMH-Plus and YHLO, AMH) be used interchangeably as a companion diagnostic for individualisation of follitropin delta dosing

Method:
The correlation of the YHLO iFlash 1800 AMH assay with the Roche Cobas e-411 AMH-Plus assay was determined by a comparative study of 151 patients at a South Australian Fertility Clinic. The degree of misclassification to different treatment categories was estimated should the YHLO AMH assay be used as a companion diagnostic instead of the Elecsys® AMH-Plus in determining the dosing of follitropin delta.

Results:
Passing-Bablok regression analysis comparing the YHLO-AMH and the Roche AMH-Plus assay resulted in a slope equation of y = 0.289 + 0.896 x (95% CI were 0.238 to 0.316 and 0.874 to 0.921, respectively) and a Spearman rank correlation coefficient of 0.984, with a 95% CI of 0.978 – 0.989. Overall, 41 women (27.2%) of patients would have been misclassified to a different treatment with 34 women (22.5%) receiving a different dose. The average dose difference was 0.98 (rate change 95% CI 0.94, 1.02) or -0.11 mcg (95% CI -0.47, 0.25mcg).

Conclusion:
The YHLO-AMH assay and the Roche AMH-Plus assay were highly correlated, with no clinically significant bias. Using the YHLO-AMH-assay would result in a modest proportion of patients receiving a different dose. Whether the dose difference is clinically significant needs to be established in further studies.

The Management of Subclinical Hypothyroidism in Infertility

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Background:
Subclinical hypothyroidism is a common disorder among women of childbearing age and may be associated with the presence of thyroid autoantibodies. Previous studies have demonstrated an association with adverse fertility and pregnancy outcomes and this condition can pose a management dilemma for the fertility specialist.

There is currently no consensus or conclusive guideline for screening infertile women for this disorder and the laboratory parameters are highly debated. In addition, there is conflicting evidence in the literature about whether the commencement of levothyroxine treatment improves fertility outcomes in women with subclinical hypothyroidism and a history of infertility. Some studies suggest that women undergoing fertility treatment with assisted reproductive technologies may be the most likely group to benefit from treatment, however, data is lacking in relation to timing, dosage and the precise subgroup of women to offer treatment to. This is an evolving area of current research with a strong focus on guiding future management of this condition in women with infertility.

The Level of Anti-Mullerian Hormone, Follicle-Stimulating Hormone and Antral Follicle Count Towards the Number of Oocyte Retrieved in Infertile Women

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Aim:
The objective of the study was to identify the the correlations between Anti-Mullerian Hormone (AMH), Follicle-Stimulating Hormone (FSH) and Antral Follicle Count (AFC) towards the number of oocyte in infertile women.

Method:
In this observational - cross sectional study, 145 infertile women, whom undergoing first in vitro fertilization cycles, were assessed in Morula IVF Makassar Clinic. Subjects were divided into three age groups: group I < 35 years (n=79), group II 35 – 40 years (n=54), group III 41 – 46 years (n=12). AMH, FSH and AFC were measured on day 2 of the patients' menstrual cycles meanwhile oocyte retrieved were measured on Ovum Picked-Up days. The data were collected from January – December 2018.

Results:
There was a significant negative correlation between age and AMH level ($r=-0.94$, $p < 0.05$), and AFC ($r=-0.92$, $p<0.05$). Meanwhile FSH level had positive significant correlation with age ($r=0.85$, $p<0.05$). AMH, FSH and AFC levels were used as markers for ovarian reserve and by using ANOVA statistical analyses, we found that the combination of three markers had the most significant correlation to number of oocyte retrieved ($r= 0.41$, $p< 0.005$), compared to AMH and FSH levels ($r = 0.35$, $p<0.05$) as well as to AFC and FSH levels alone ($r=0.30$, $p<0.05$).

Conclusion:
AMH, FSH and AFC has been used as an individual or combined markers for ovarian reserve. From this study we found that the combination of the three markers shows a significant improvement in predicting the ovarian function as can be shown from the number of oocyte retrieved.

HLA Matching

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Abstract:
Human Leukocyte Antigen (HLA) refers to a particular gene complex on chromosome 6 that plays a critical role in the immune system. HLAs are involved in presentation of foreign antigens to enable specific activation of T cells and immune rejection, and are themselves subject to surveillance by the immune system to differentiate self from foreign invaders. As human pregnancy is a case of invasion of the uterus by an antigenically-foreign fetus, special adaptations have been necessary to enable the fetus to survive. Over the last 60 years our understanding of this topic has grown exponentially, and taken strikingly surprising directions. We know that HLA differences are detected by the olfactory system and humans and other animals seek out mates with different HLAs to themselves. We know that survival of the fetus is improved by HLA differences, in marked contrast to surgical tissue transplants for example. We know that some placental cells do express HLAs which actively engage with uterine natural killer cells, and this interaction likely forms the basis for the maternal adaptation to pregnancy. These and other findings have formed the theoretical basis for various immune therapies for reproductive failure, and the concept of HLA matching is likely to become more prominent as it can lead to more specific targeting of either none or different types of immune therapy. This talk will aim to give a fertility specialist the basic information needed to appreciate our understanding of HLA compatibility (A, B, D), HLA-G and HLA-C interactions with natural killer cells.

The Development and Pilot Testing of a Decision Aid for Women Considering Elective Egg Freezing

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Background:
The decision to freeze eggs for non-medical reasons can be complex. Women are weighing up the costs, side-effects and the uncertainty of outcomes against their personal situation and desire to be a parent in the future. With no clear medical best option, the decision is a values-based one. The gold-standard intervention for such decisions is a Decision Aid which has been shown to facilitate informed decision-making.

Aim:
To develop an online, interactive Decision Aid for women considering elective egg freezing and to pilot test it for acceptability and usefulness.

Method:
Australian women aged 18-45 years and interested in receiving egg freezing information were recruited through social media to complete pre/post surveys that assessed the impact of the Decision Aid on uncertainty (decisional conflict), knowledge, acceptability (including, satisfaction and relevance), and usefulness.

Results:
Twenty-seven women participated. Post review of the Decision Aid, participants had significantly reduced decisional conflict ($p=0.002$) and improved their knowledge ($p=0.047$). The vast majority (93%) found the Decision Aid to be acceptable, with 96% reporting satisfaction with the tool, and 88% finding it helpful in explaining their options. Most (88%) would recommend the Decision Aid to others. However, it was identified that there was still a need for specific details that can only be sourced from clinical consultation.

Conclusion:
Participants were generally positive about the Decision Aid. It was acceptable, useful and appeared to improve knowledge and reduce uncertainty (which clinically manifests in decision delay). The Decision Aid may be a useful supplement to clinical discussions. Next step is to perform a randomised controlled trial to evaluate efficacy.

Exploring the Knowledge and Decision-Making Needs of Women Interested in Receiving Information About Elective Egg Freezing

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Background:
Advances in egg freezing technology mean women now have the opportunity to potentially extend their reproductive lifespan. The decision to freeze however is complex and requires consideration of many factors, including costs, side-effects and the uncertainty of outcomes. To best support women, we need to understand women's knowledge of egg freezing, and what information they need to make an informed decision about whether to proceed.

Aim:
To explore women's knowledge of egg freezing, time spent searching for information, importance of being informed about egg freezing, need for information and support, uncertainty around the decision (decisional conflict), and preferred format for information delivery.

Method:
Australian women aged 18-45 years interested in receiving egg freezing information were recruited through social media to complete an online cross-sectional survey.

Results:
The survey was completed by 332 participants. Total mean knowledge score was 8.7/13 (SD 2.7). Poorly answered questions related to the number of eggs needed to have a high chance of a live birth, and the ability to measure egg quality before a cycle. Most women (81%) had high decisional conflict. Univariate analysis also showed a strong association between consulting a fertility specialist and higher knowledge ($p<0.0001$), and lower total decisional conflict scores ($p<0.0001$). Most participants (85%) disliked the term 'social egg freezing', and most (70%) considered 'elective egg freezing' as the best term to use.

Conclusion:
Participants were generally well informed about egg freezing however they showed a poor understanding of certain areas. Decisional conflict overall was high which can manifest into decisional delay. Consulting a fertility specialist appears to improve women's knowledge and ability to decide on egg freezing. Finally, terminology used to describe egg freezing should be sensitive to women's experiences.

What is the Utility of a Cannulated Prolactin Study in Women Presenting with Infertility?

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Background:
The prevalence of hyperprolactinaemia in women presenting for infertility investigation has been found to be up to 17%, and many of these women are asymptomatic. A raised prolactin concentration adversely affects fertility by reducing gonadotropin secretion by inhibiting gonadotropin releasing hormone from the hypothalamus. However, prolactin may be elevated through stress, including phlebotomy and may not be of clinical significance. A cannulated prolactin series may be a useful way to discriminate this.

Aim:
To investigate the true prevalence and positive predictive value of elevated prolactin in women presenting for infertility investigation following a cannulated prolactin study and the initial investigation results.

Method:
All women referred to two fertility centres in Wellington, NZ had prolactin measured prior to first appointment. If the prolactin was elevated on two occasions, they were referred to Endocrinology for a cannulated prolactin series which involves the insertion of an intravenous cannula and five blood samples drawn over two hours. If the prolactin falls within the reference range during the series this is regarded as normal.

Results:
1660 women across both centres were seen for a first specialist fertility appointment during the study period. Forty four (3%) had persistently raised prolactin concentrations after two samples and were referred for a cannulated study. The positive predictive value for raised initial prolactin being truly raised was 38.64%. Even in patients with a prolactin of greater than 1000 (reference range 100-500mU/L), 45% had a normal two-hour cannulated study. No correlation was found between the concentration of the initial prolactin and an elevated two-hour concentration.

Conclusion:
The prevalence of raised initial prolactin was 3% in our population. A two hour cannulated prolactin study identified those women with a truly raised result requiring further investigation. The initial concentration has a low positive predictive value for those having a truly raised prolactin.

What's the Point of Sex?

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Abstract:
With the success of assisted reproduction, one may ask whether sex for procreation has become redundant. Indeed, IVF overcomes many barriers that natural conception poses. But one element of sex isn't recapitulated by IVF - the female immune response to the male partner's seminal fluid. Why does that matter? Increasing evidence suggests a couple's sexual activity and in particular, transmission of seminal fluid, are important for conditioning the female immune response to assist receptivity and support embryo implantation. Historically, seminal fluid has been viewed as simply a sperm transport medium. But seminal fluid has a more complex function in orchestrating a complex communication with the female immune system, to directly influence female reproductive physiology.

Studies in laboratory models have unraveled the mechanisms by which this occurs. We and others have shown that seminal fluid carries potent signaling agents, which interact with the female reproductive tissues to alter gene expression in the cervix, uterus, oviduct, ovary, and potentially even the hypothalamic pituitary axis. The net result is to induce cytokines and stimulate immune cells, promote ovulation and corpus luteum formation, enable robust embryo development and implantation, and ensure optimal placental development. Seminal fluid contact not only improves fertility, but also influences fetal programming and offspring health.

These findings in animals have led to the question of whether seminal fluid might increase the chance of successful conception and pregnancy in assisted reproduction treatment cycles in women. While appropriately powered clinical studies to provide conclusive evidence are lacking, recent meta-analyses assembling evidence from >2400 women show that sexual intercourse or assisted delivery of seminal fluid can increase conception rates after IVF embryo transfer cycles by 20% or more. At a biological level, studies examining the human female response to seminal fluid reveal it transmits immune-regulatory factors that induce expression of genes and microRNAs, which are known to promote immune tolerance for pregnancy.

While intercourse during an IVF/ET cycle is not essential for pregnancy after IVF conception, the balance of evidence suggests seminal fluid exposure is beneficial. Encouraging coitus where appropriate may be a safe, simple and low-cost way of improving the chances of success. Future studies to determine the mechanisms by which seminal fluid interacts with female reproductive tissues will provide better understanding of the immune mechanisms governing normal fertility, and help determine how the immune response contributes to subfertility disorders.

Clinical Experience of Large ART Program in Japan - Hanabusa Womens Clinic (How we Manage Around 6000 Cycles of OPU/9000 of FET a Year)

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Hanabusa Women's Clinic, Kobe,Japan

Background:
Japan has more than 600 ART registered facilities, and 447790 cycles of treatment were performed in 2016, resulting in the birth of 54,110 children. It can be said that Japan is one of the world's leading ART countries. As a feature of Japan's ART facilities, there are many relatively small facilities and 82.6% of all children born afeter ART treatment are derived from freeze-thawed embryo transfer. In 2016, there were only 2 facilities in Japan that performed freeze-thawed embryo transfer over 3000 cycles, and our reproductive center is one of them. In this lecture, I would like to consider the know-how of our reproductive center. The first one is about how to improve doctors' skills, the second is about building a system that supports smooth operation of the large center, and the third is about advocating a medical philosophy that can be shared by each staff member. Regarding the doctor's knowledge and technics, I would like to emphasis embryo transfer is an important technique that may affect treatment outcomes directly. Therefore, in this lecture, we will introduce our “Excellent” embryo transfer and our “Challenge” up to that point.

As the second theme,I would like to introduce our “Computer network construction”. In our reproductive center, the database created by electronic medical records and database is operated by configuring a network with 120 terminals installed in our facility. We think that it is essential that all the staff can instantly share a lot of complicated information that can be linked to each patient. In order to realize tailor-made and detailed treatment for each patient, an environment that allows easy access to current and past information of patients is necessary. In our case, “Challenge” for better “system construction” never ends.

The third point in this talk is advocating the medical philosophy. Needless to say, "Excellent ART" is not something that can only be accompalished by physicians, but it is achieved for the first time by a team collaborating organically. In order to create such a team, it is necessary to have a medical philosophy that can be shared by staff. In our reproductive center, all staff members are advocating the medical philosophy in three forms: “credo for patients”, “credo for staff” and “quality policy”. In this talk, I will introduce the medical philosophy of us in detail, and will also introduce a method for instilling this medical philosophy into the staff.

The Endometrial Microbiome Exist and Matters

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Background:
The discovery of microbial communities inhabiting the whole female reproductive tract has challenged the traditional view of human fetal development in a sterile environment. Technical advances have facilitated the study of the bacterial microbiome in the upper and lower genital tract, as well as the role of such bacteria in women's health and fertility

Aim:
The microbiota in the urogenital tract of healthy reproductive age women is mainly composed of bacteria from the Lactobacillus genus (1); however, structural or compositional variations of this microbiota, that could occur throughout a women's life in response to intrinsic and extrinsic factors may impact the function of reproductive organs. Non-lactobacilli dominant uterine microbiome in the uterine cavity has been associated with poor reproductive IVF outcomes, by increasing implantation failure and miscarriage (2). This presentation will focus on the current knowledge of the endometrial microbiome and their functional relevance in the reproductive process

Method:
We will present the current knowledge of the endometrial microbiome base on next generation sequencing, functional bioinformatics and clinical outcomes

Results:
Non-lactobacilli dominant microbiome in the uterine cavity has been associated with poor reproductive IVF outcomes, by increasing implantation failure and miscarriage (2). For this reason, assessment of the endometrial microbiome has been proposed to be considered in infertile patients with implantation failure to improve our understanding and develop personalized strategies to improve clinical results

Conclusion:
The investigation of endometrial bacterial communities has revealed that the endometrial cavity is not sterile. The knowledge of the reproductive microbiome will add a new angle for the understanding of the reproductive function

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Non-Invasive PGT-A; the Next Generation for Embryo Viability Diagnosis

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Background:
The success of assisted reproduction treatments is based on the selection of the best embryos for transfer, those with the highest implantation potential and ongoing pregnancy rates: euploids. The most reliable method to assess the chromosomal status of preimplantation embryos is preimplantation genetic testing for aneuploidies (PGT-A). Other options such as morphology and morphokinetics are not good candidates to replace PGT-A techniques as their correlation with embryo ploidy is weak. However, biopsy-based approaches on PGT-A entail both technical and economic challenges as embryo manipulation is needed and it could affect viability. To avoid those limitations, non-invasive methods based on the analysis of the cell-free DNA released by the embryo during the latest stages of preimplantation development has been proposed.

In the last years there have been different attempts to overcome trophectoderm biopsy to diagnose the chromosomal content of the embryos. Some groups started with the analysis of blastocoel fluid obtained by aspiration with a thin micropipette as a less invasive approach than TE biopsy. Later on, some groups proposed a “true” non-invasive approach consisting in the study of the spent culture media to analyse the embryonic cell free DNA (cfDNA) released by the embryo during the latest stages of preimplantation development. After the first publications, several studies have compared the results of PGT-A in TE biopsies with the results of the spent culture media, to establish the concordance rates among both approaches. In these studies, the percentages of informative samples vary widely, likely reflecting the existence of mosaicism and/or presence of DNA from granulosa, cumulus cells or polar bodies in the spent blastocyst media (SBM) urging the need for technical improvements before this new non-invasive technology can be clinically applied

Aim:
To address the two main limitations of current PGT-A, namely invasiveness and diagnosis of mosaicism using non-invasive PGT-A analysis of the embryonic cell free DNA (cfDNA) released by the embryo during the latest stages of preimplantation development.

Method:
We have conducted a pilot study comparing aneuploidy testing using a non-invasive approach to trophectoderm biopsy, advancing one step towards understanding the potential value of niPGT-A in embryo cell-free DNA. Regarding clinical outcome, we have followed-up data on a subset of patients after SET performed according to TE biopsy results and compared the clinical outcome retrospectively according to cfDNA results

Results:
Concordance rates between both techniques are superior to 80%. Interestingly, ongoing implantation rates are 3-fold- increase when both TE and cfDNA were euploid, compared to euploid TE paired with aneuploid cfDNA, indicating that embryonic cfDNA might open a new avenue for the understanding of embryo ploidy.

Conclusion:
The origin of embryonic cfDNA is still unclear but due to the high concordance (>80%) and improved clinical results this is a promising new technology that might circumvent certain limitations of PGT-A.

Endometrial Receptivity - "The Devil is in the Details"

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Background:
Personalized medicine is a well-accepted concept in reproductive medicine except for the endometrial factor that is still neglected. Endometrial receptivity refers to a hormone-limited period in which is acquired a functional and transient status allowing blastocyst adhesion. We have developed the endometrial receptivity analysis (ERA) (1,2) based on the transcriptomic signature of 238 genes now using Next Generation Sequencing (NGS) coupled to a computational predictor capable of diagnosing the window of implantation (WOI) regardless of its histological appearance. Its accuracy is superior to endometrial histology and reproducible 29 to 40 months later (3). Currently, this test is indicated in patients with implantation failure (IF) of endometrial origin, through personalization of the day of embryo transfer (pET) (4-8). Here, we present a clinical update about the use of ERA worldwide.

Aim:
To discuss the ERA clinical concept, which is personalization and synchronization, guiding a personalized embryo transfer (pET) by synchronizing the embryo with the WOI of the patient in a personalized manner.

Method:
Basic research, evidence-based medicine clinical trials from case reports, retrospective, prospective and RCT to investigate the reproductive outcome in infertile women under 38 year in their first IVF/ICSI cycle with elective blastocyst transfer.

Results:
According to all clinical data gathered, personalization of the endometrial factor using molecular objective diagnosis improves clinical results in patients with implantation failure of endometrial origin.

Conclusion:
Personalization and molecular diagnosis of the endometrial window of implantation has potential to improve our clinical practice.

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Sperm Selection and its Influence on the Resulting Embryo

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Abstract:
The conditions for embryo culture and the selection of the best euploid embryo for transfer are often the main focus of research and improvements in ART. The spermatozoon increasingly finds itself at the bottom of the embryologists priority list.

This presentation will aim to lift the status of the sperm and raise awareness of its importance in achieving good fertilisation, embryo growth and perfect embryos to transfer.

The road to sperm care starts at the time of ejaculation, when time to preparation becomes crucial for the outcome. Extended exposure of sperm to seminal fluid will negatively affect the sperm through oxidative stress, which in turn can lead to increased DNA damage and possibly effect mutational load in the offspring. A number of methods are available for preparing sperm, some more suitable than others when taking the resulting embryo into account.

After the preparation the sperm will hopefully be suspended and used for conventional IVF, allowing for a natural selection of sperm when meeting the oocyte. However in approximately 35% of cases ICSI is required to assure safe fertilisation, and the embryologist will choose the best sperm rather than nature. What criteria are there for selection of the best and how does this selection affect the morphology, euploidy and developmental capacity of the resulting embryo?

Finally there are the very few but difficult cases, where it is hard to find sperm, leaving embryologists searching ejaculates or testicular tissue. In these cases the process of preparation and sperm selection becomes even more important for the outcome.

By paying attention to all aspects of sperm handling and selection we can improve our results and remember, “Every sperm is sacred”!

Don’t Judge a Book by its Multinucleation

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Aim:
To investigate the impact of multinucleation on ART outcomes.

Method:
A total of 2495 embryos were cultured in Embryoscope+ and analysed for multinucleation at the two and four cell stages. Assessment included number of blastomeres multinucleated and the number of nuclei seen. Morphokinetic parameters were assessed and utilisation and clinical pregnancy results examined. All embryos were cultured to blastocyst, and all transfers were single embryos.
To emulate the observation of multinucleation in laboratories not using time-lapse incubation embryos were also assessed at 42 hpi, with presence or absence of multi nucleation noted at this static timepoint.

Results:
Neither occurrence nor type of multinucleation was impacted by female age, appearance of sER discs, uneven pronuclei or uneven two cell blastomeres.
Multinucleation was observed in 31.6% of embryos under time-lapse, of this sample 8.1% were visible at 42 hpi. Multinucleation was more frequently observed at two cell stage compared to four cell stage (25.6%v11.2% respectively;p=0.0001).
Multinucleation seen at two cells persisted into the four cell stage in 20.1% of embryos. These embryos displayed significantly lower utilisation compared to those with multinucleation only at the two cell stage (24.7%v43.5% respectively;p=0.003).
Embryo development as indicated by time to cavitation (both absolute and relative to syngamy) was not affected by the presence of multinucleation (102.0v102.5hpi respectively;p=0.7). Interestingly, clinical pregnancy rates displayed no difference in embryos without multinucleation compared to multinucleated (36.5%v33.3% respectively;p=0.8). Reassuringly, multinucleation also appears to have no impact on miscarriage rates (11.1% for multinucleate embryos and 21.4% for those not multinucleated;p=0.5).

Conclusion:
Multinucleation seems to have no negative impact on embryo development nor the embryo’s ability to implant and sustain a viable pregnancy. Multinucleation assessment should be reconsidered as a non-vital parameter for embryo assessment.

Characteristics of Human Single Pronucleated Zygotes Derived From Conventional *in Vitro* Fertilization, Considering the Genome Composition, Chromosomal Distribution and Morphological Assessment

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Background:
An oocyte showing two pronuclei/ two polar bodies (2PN/2PB) is considered “normally fertilized” in assisted reproductive technologies. Meanwhile, zygotes with a single pronucleus (1PN) are often encountered in clinical settings. In previous studies, cytogenetic and genetic composition based on histone modification analysis has revealed that many 1PN zygotes are diploid in conventional in vitro fertilization (c-IVF) procedures. Furthermore, some of these zygotes can develop to blastocysts and produce normal deliveries in humans. Nevertheless, the characteristics of human 1PN zygotes derived from c-IVF remain unknown.

Aim:
To non-invasively validate the developmental potential of human c-IVF 1PN zygotes at the zygote stage.

Method:
We used c-IVF 1PN zygotes obtained from February 2015 to September 2017 (n= 60). Immunohistochemistry and fluorescence live-cell imaging were used to confirm normal chromosome segregation during first cleavage. The usefulness of measuring pronuclear diameter was assessed on the basis of the presence or absence of a proper first cleavage and validated by subsequent development.

Results:
Although approximately 80% of c-IVF 1PN zygotes contained a diploid genome, immunohistochemistry revealed an unequal distribution of paternal and maternal genomes at the first mitosis. Fluorescence live-cell imaging revealed that 73% of 1PN zygotes formed a functional mitotic spindle at the first mitosis resulting from diploid genomes, with 18% of these forming a tripolar spindle. 1PN zygotes in which the pronucleus disappeared and that subsequently underwent cleavage had a pronuclear diameter ≧32.2 μm. The selecting 1PN zygotes based on pronuclear diameter resulted in zygotes that all formed mitotic spindles with poles during cleavage. Furthermore, 80% of these zygotes reached the blastocyst stage.

Conclusion:
This study demonstrates the usefulness of a non-invasive assessment of c-IVF 1PN zygotes. A pronuclear diameter ≧32.2 μm just before PN breakdown might be a useful criterion to assess 1PN zygotes that are capable of further development.

An Australasian Ovarian and Testicular Tissue Cryopreservation Transportation Program.

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Background:
Fertility preservation strategies (FPS) widely available include oocyte and embryo cryopreservation. Ovarian tissue cryopreservation is now also acknowledged as being clinically useful, particularly as it is the only option for children and prepubescent girls. Testicular cryopreservation remains experimental for boys, but has the potential to provide a realistic opportunity for fertility in the future. However gonadal tissue cryopreservation (GTC) requires particular scientific and laboratory expertise. Young cancer patients seeking fertility preservation may not be currently afforded the opportunity because of lack of accessibility. One approach is to provide a national tissue retrieval and transport service. Robust protocols confirming tissue viability after transport have been published[1,2].

Aim:
The establishment of a GTC transport program, allowing local comprehensive oncofertility service provision and referral for transport, processing and storage in a centralised centre with specific expertise.

Method:
An information/education/instruction resource is developed for fertility units Australia-wide, supported by a centralised GTC program manager. Gonadal tissue is retrieved at the local centre and then transported. Tissue is cryopreserved and stored for future use. Subsequent grafting be performed either locally or centrally.

Conclusion:
Provision of a FPS for young people, as mandated by national and international guidelines, requires accessibility to GTC, which is currently not widely available. Tissue transport would facilitate engagement and upskilling in oncofertility with high-level support from a centre of excellence, allowing expansion of patient and provider access to best-practice options, regardless of geographic location.

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Controlled Ovarian Stimulation in Breast Cancer Patients: Does Receptor Status Make a Difference?

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Background:
Fertility preservation (FP) protocols include tamoxifen for controlled ovarian stimulation (COS) in patients with estrogen receptor-positive (ER+) breast cancer, to reduce the breast tissue exposure to estrogen.

Aims/Objectives:
To evaluate COS outcomes, such as oocyte yield, mature eggs frozen, recombinant FSH dose and duration of stimulation between the ER+ and estrogen receptor negative (ER-) groups, due to tamoxifen exposure.

Methods:
In this retrospective cohort analysis, 204 breast cancer patients (146 ER+, 58 ER-) presenting for FP between 2013 – 2018 were studied. Eighty of these patients underwent embryo freezing, while mature egg freezing was performed in the remainder (124 patients). The patients underwent antagonist cycles, with tamoxifen administered for the duration of stimulation in the ER+ group.

Results:
The patients had a mean age of 35.1 and 33.3 years in the ER+ and ER- groups.
We observed no significant differences in the ER+ and ER- groups, with respect to mean eggs collected (13.2 and 11.8, respectively), FSH starting dose (253.3 and 251.9 IU), duration of FSH (13.8 and 13.2 days). Interestingly, there was a statistical difference in the mean number of mature eggs frozen (12.3 and 9.4, p-value 0.05), favouring the ER+ group and cannot be attributed to age. The mean number of embryos frozen was the same for the two groups (4.9 and 4.6).

Conclusions:
While a higher number of mature eggs were frozen in the ER+ group, for those patients undergoing embryo freezing, the mean number of embryos frozen were the same for the two groups. COS outcomes were similar for patients with breast cancer, irrespective of receptor status and co-treatment with tamoxifen.

Recurrent Miscarriage – An 18 Month Review

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Background:
Recurrent pregnancy loss (RPL) as defined by the American Society of Reproductive Medicine (ASRM) and European Society of Human Reproduction and Endocrinology (ESHRE) is the loss of two or more pregnancies at less than 24 weeks' gestation. It affects 1-5% of couples trying to conceive.

The Recurrent Miscarriage Clinic (RMC) at Royal Prince Alfred Hospital (RPAH), a tertiary hospital in Sydney provides counselling and investigation for couples affected by RPL. To date no analysis of patients using this service has been performed.

Aim:
To analyse demographics, aetiology, and pregnancy outcomes in patients presenting to the RMC.

Method:
Retrospective review of patients presenting to the RMC at RPAH, Sydney from January 2018 to May 2019. Inclusion criteria were any patient attending the RMC affected by RPL as defined by ASRM/ESHRE. Data was extracted from electronic medical records. Institutional ethics approval was obtained (approval number: X18-0247).

Results:
32 couples were seen between January 2018 and May 2019 (total 54 visits). The average age of the female patient was 34 years (range: 24 to 42 years). The mean number of pregnancy losses on initial referral was 3 (range 2 to 7). In 53.1% of cases, no cause for RPL was found on investigation. 18.8% of women achieved a subsequent live birth with a further 9.4% pregnant at the time of data collection.

Conclusion:
The RMC sees a diverse range of women. Results are in keeping with other studies which show that RPL is unexplained in 50-75% of cases. Outcomes are encouraging, showing that almost 20% of women achieved a live birth within a short period of being assessed. Ongoing follow-up is required to ascertain long-term pregnancy outcomes for the cohort.

Two is Better than One? Would Elective Single Blastocyst Transfer be a Better Option in IVF?

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Background:
Double blastocysts transfer (DBT) have been shown to improve pregnancy rates in comparison with single blastocyst transfer (eSBT), however the risk of having multiple pregnancy remains high.

Aim:
To evaluate clinical outcomes of eSBT versus DBT in patients who had cryopreserved all blastocysts in fresh cycle, followed by their first vitrified-warmed cycle.

Method:
156 cases from 2015-2018 were reviewed retrospectively. Two main groups being studied, eSBT (n=30) and DBT (n=126). Preimplantation genetic screening cycles were excluded. All IVF/ICSI embryos were cultured to blastocyst stage. Patients who developed ≥2 full blastocysts, scored at least BB quality (Gardner's grading system) or better, had all blastocysts cryopreserved in fresh cycles and transferred in subsequent frozen embryo transfer (FET) cycle only were included in analysis. Blastocysts were considered as transferrable if >80% cells remained intact after warming. Statistical analyses were performed using fisher exact and t-test.

Results:
The risk of multiple gestation was noticeable higher in DBT group compared to eSBT group (33.3% vs 0%, p=0.0001). No significant difference in clinical pregnancy rate (CPR), implantation rate (IPR) and live birth rate (LBR) in eSBT vs DBT respectively (43.3% vs 61.9%, p>0.5) (43.3% vs 41.6%, p>0.5) (43.3% vs 47.6%, p>0.5). The mean age of eSBT group was 33.8±5.8, while DBT group was 30.3±5.3 (p=0.004).

Conclusion:
Our study showed that eSBT appears to have significant lower multiple pregnancy risk. eSBT group patients were slightly older in this study, yet able to produce comparable CPR, IPR and LBR by transferring one blastocyst only. Therefore, eSBT should be promoted as it is safer option to minimize the risk of multiple gestation without compromise the positive clinical outcomes.

Towards Automation of the IVF Laboratory

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Aim:
Automation replaces techniques that people perform, as it reduces human error through reducing variation in technique. The more sophisticated yet routine the technology, the more value automation provides, if successfully delivered. The IVF laboratory is an exemplary target for automation, as much of what occurs within the lab is both highly skilled but also routine. Examining how far we have come towards the automated IVF laboratory and where it could take IVF practice is the goal of this presentation.

Methods:
Analysis of literature reveals 3 primary areas where automation can be applied: assessment of oocyte/embryo quality; improvement of embryo environment to improve production, which must focus on improving the embryo quality; and lastly, the protection against accidental mixed parentage.

Results:
Rapid progress has occurred in the application of machine learning algorithms associating either single or time-lapse images of embryos to developmental outcomes, including ploidy state and implantation success. Other areas include automation of gamete and embryo parental identification, and cryopreservation processing. Whole laboratory management systems will provide the “paperless” IVF clinic. Missing is automation of the fertilization, embryo culture and other manipulation processes, but this too is being addressed through research.

Conclusion:
Over the next decade, there will be further automation in the IVF laboratory, to the point where much of the processes will come together in a single device. Artificial intelligence and robotic capabilities will be the new tools, and improvements in patient outcomes will be remain the aspirational goal.

Clinical Validation of Automated Semen Analysers Versus Conventional Analysis.

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Background:
It is important as new automated semen analysers enter the consumer market to perform clinical validation studies.

Aim:
To simultaneously compare key semen parameters between two commercially available automated semen analysers and conventional semen analyses.

Method:
A total of 69 sperm samples were split into three aliquots and simultaneously evaluated for sperm concentration and total motility using 1) commercially available automated semen analyser one 2) commercially available automated semen analysis two and 3) Conventional semen analysis (by two experienced embryologists). The 69 sperm samples were tested irrespective of semen quality. The performance of the two commercially available automated semen analysers along with conventional semen analysis were evaluated by comparing the median (± standard deviation), R^2 values, and relative deviations in the semen parameters obtained by the three methods.

Results:
The median (± standard deviation) sperm concentration was 39.7M/ml, 60.8M/ml and 32.2M/ml for analyser 1, analyser 2 and conventional assessment respectively. The median (± standard deviation) total motility was 51.0%, 67.0% and 56.7% for analyser 1, analyser 2 and conventional assessment respectively. R^2 values for all combinations of total motility were below 0.2, indicating poor correlation between all three methods. Similarly, R^2 values for all combinations of concentration were below 0.6, still indicating a relatively poor correlation between all three methods. Relative total motility deviations of ≥30% were seen frequently between the two commercially available semen analysers (32.1%), and also between conventional assessment and analyser 2 (22.6%), whereas conventional assessment and analyser 1 has the highest agreement rate (17%). Relative concentration deviations of ≥100 M/ml were seen between the two commercially available semen analysers (10.1%) and also between conventional assessment and analyser 2 (17.4%), whereas no sample had a deviation of ≥100 M/ml between conventional assessment and analyser 1 has the highest agreement rate (0.0%).

Conclusion:
Differences across all three methods were observed however there were large differences in parameters detected in one of the automated methods in particular, questioning the need for further validation of this unit.

3 Person IVF and Mitochondrial Haplogroups

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Abstract:
Reproductive options for families affected by mitochondrial DNA (mtDNA) disease are complicated by the quirky genetics of mtDNA: maternal inheritance, mtDNA copy number (~200,000 in mature oocytes), heteroplasmy (mixture of wildtype and mutant genomes), the threshold effect (proportion of mutant mtDNA required to cause dysfunction) and the bottleneck effect, whereby a female carrier can have eggs with mutant loads ranging from 0% to 100% and anywhere in between. Oocyte donation is a potential option for any couple and, for women at relatively low recurrence risk, prenatal diagnosis or PGD can be good options.

Mitochondrial Donation (or Mitochondrial Replacement Therapy) could potentially allow any couple at risk for transmitting mtDNA disease to have a healthy child who is genetically related to both parents. It remains illegal in most jurisdictions and the Government response to a 2018 Senate Inquiry notes it may provide a valuable additional option and has initiated further consultation. One concern has been whether mtDNA haplogroup matching should be required to avoid any possibility of an incompatibility between donor mtDNA and the parental nuclear genomes. Requiring matching could impact markedly on availability of a suitable egg donor as many haplogroups are uncommon in the population. I will discuss data from flies, mice, monkeys and humans, including culture of embryonic stem cells from human embryos that have undergone mitochondrial donation. Like the UK HFEA, I believe this issue should be included in genetic counselling of couples but that the risks of a compromised outcome remain too low to require matching.

Can (and Should) a Doctor Tell my Biological Relative My Genetic Results Without My Consent?

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Abstract:

Genetic changes that cause health complications can be hereditary, meaning genetic information is relevant not only for an individual but also their blood relatives. However, notions of medical privacy and doctor-patient confidentiality have traditionally been understood to mean that medical professionals owe duties to and should consider the relevance of information only to their own patient.

In the UK, a woman recently sued a London hospital for doctors not disclosing that her father had the genetic mutation that causes Huntington disease – a neurodegenerative disorder. The woman was pregnant at the time. She argues doctors should have told her about her risk of also having the mutation and passing it on to her unborn. The UK case raises the question of whether medical professionals have a duty to disclose a patient's genetic test result to family members who might be at risk, even without consent.

No such legal case has arisen in Australia to date. If it did, there are some laws governing the disclosure of genetic information that could be relied on. But these are inconsistent and information about how often medical professionals do rely on them is lacking. This presentation will consider these issues, the laws that are in place in Australia, and whether medical professionals have a duty to consider genetic relatives in making an assessment regarding disclosure.

Cost-Effectiveness of Assisted Reproductive Technology for Couples with Unexplained Subfertility: When to Treat?

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Background:
Assisted reproductive technology (ART) such as intrauterine insemination (IUI) and in vitro fertilisation (IVF) are often used for couples with unexplained subfertility despite the fact that there is not a clear diagnosis which these treatments aim to overcome. Couples with unexplained subfertility can still conceive naturally and ART thus may be an unnecessary, invasive and stressful procedure that is expensive and increases the chance of a multiple pregnancy. The year by year escalation in terms of the number of ART cycles conducted represents an increasing financial burden to public health services, if ART is (partly) reimbursed. Clinicians and public health services are uncertain how to deal with this pressing issue and how the group of unexplained subfertile can best be managed. Couples may first pursue expectant management (EM) for a longer period of time, then start IUI and only start IVF if the first two options did not result in a baby. Alternatively, couples could start ART straightaway. We require evidence in terms of the cost-effectiveness of these various scenarios for the choice and ordering of ART treatment for unexplained subfertility.

Aim:
To construct an economic model that weights the pros of ART, i.e. the increased chance of achieving live birth, to the cons, i.e. costs and the increased chance of multiple gestations.

Method:
We developed a Markov decision analytic model that follows couples with unexplained subfertility up to a female age of 38 years from completion of the fertility workup for the next 3 years. We chose the Dutch societal perspective, but the model is easily modified for other locations or perspectives. We divided the time axis of 3 years into three separate periods, each comprising 1 year. We changed the order of ART treatment for the 1 year periods to yield different treatment scenarios, for instance the order EM, IUI, IVF or IVF, EM, EM. The chances of natural conception were taken from the dynamic prediction model for natural conception and updated for years 2 and 3. The relative effects of ART treatment in terms of odds ratios were taken from a network meta-analysis and are applied to the chance of natural conception. We applied standard discounting procedures for economic analyses for the time period of 3 years using discount rates from the Dutch government. The uncertainty around ART treatment effectiveness, costs and other parameters was assessed by probabilistic sensitivity analysis in which we drew values from distributions and repeated the procedure 1000 times.

Results:
Results suggest that the order IUI, IVF, EM is the most effective but also the most expensive and leads to the highest proportion of multiple pregnancies. The order EM, IUI, IVF was dominated by IVF, EM, EM as the latter was both more effective and less expensive. Up to a willingness to pay of approximately €20.000 per live birth, the order EM, EM, IVF is the most cost-effective in terms of net benefit. For €25.000 or higher, the order IVF, EM, EM is the most cost-effective. The combination of both IUI and IVF treatment does lead to higher chances of live birth but this increase seems unlikely to be cost-effective.

Conclusion: We should reconsider how we clinically manage couples with unexplained subfertility. The results of our study can be used by public health services to decide on a treatment protocol based on the chance of live birth, the costs and the cons of ART treatment. Our model used contemporary evidence as its basis and is easy to apply in other countries to aid decision making.

The Effect of Thyroid Autoimmunity on IVF/ICSI Outcomes

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Background:
Thyroid autoimmunity (TAI) – the presence of anti-thyroid peroxidase and/or anti-thyroglobulin antibodies – affects 8-14% of reproductively-aged women. It is hotly debated whether TAI adversely affects IVF/ICSI outcomes. A prominent systematic review identified a marginal, but significant, negative effect of TAI on miscarriage and livebirth rates (LBR)(Busnelli et al. 2016 *Hum Reprod Update*). However, this study lacked clear definitions (e.g. miscarriages included biochemical and clinical losses; LBR did not consider per-cycle outcomes etc.). Importantly, in Busnelli et al.(2016), TAI-positive women were significantly older than TAI-negative women and some of the included papers did not report age. Since then, large studies have been published.

Aim:
To perform a systematic review and meta-analysis of the relationship between TAI and clinical pregnancy miscarriage rates (MR), ongoing pregnancy rates (OPR) and LBR during IVF/ICSI using uniform criteria and known female age.

Method:
We followed PRISMA guidelines. PROSPERO registration:CRD42019120947. Searches were undertaken in MEDLINE, EMBASE, Web of Science and Cochrane Database from Inception-April 2019. Primary outcomes were MR, OPR (per-cycle and per-clinical pregnancy [CP]) and LBR (per-cycle and per-CP). Secondary outcomes were age and clinical pregnancy rate (CPR). Quality was assessed using the Newcastle-Ottawa Quality Assessment Scales. Pooled effect sizes were estimated by applying random effects meta-analysis using Stata 15. We analysed heterogeneity (I^2), sensitivity and publication bias (Egger's weighted regression).

Results:
13 studies were included for the meta-analysis. Compared with TAI-negative women, TAI-positive women had similar MR (Odds ratio [OR]0.74; 95%CI [0.46-1.19];P=0.212;7 studies I^2=0.0%), CPR (OR 0.90;95%CI [0.76-1.05];P=0.171;9 studies;I^2=0.0%), OPR per-cycle (OR 0.89;95%CI [0.75-1.06];P=0.198;9 studies;I^2=0.0%), OPR per-CP (OR 1.35;95%CI [0.84-2.17];P=0.212;7 studies;I^2=0.0%), LBR per-cycle (OR 0.84;95%CI [0.67-1.06];P=0.145;5 studies;I^2=1.7%) and LBR per-CP (OR 0.92;95%CI [0.57-1.48];P=0.722;3 studies;I^2=0.0%). Mean ages of TAI-positive and TAI-negative women were similar (SMD 0.14;95%CI [-0.02-0.30];P=0.086;12 studies;I^2=77.2%).

Conclusion:
In women of comparable ages, TAI does not adversely affect IVF/ICSI pregnancy outcomes.

Handling the Zona Free Patient: Use of Time Lapse Incubation and Single-Step Culture to Achieve a Viable Pregnancy in a Zona Free Patient.

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Background:
Total absence of the zona pellucida (ZP) has been reported in literature with few live births reported (Stanger *et al*, 2001). It is well established that ZP is an important component of the oocyte and plays a role in oocyte metabolism, sperm interaction and subsequent embryo development (Rankin and Dean, 1996).
The ZP provides a protective barrier during the additional handling and manipulation of IVF procedures in the laboratory. Oocytes with damaged or absent ZP are highly susceptible to damage and lysis. Therefore patients who are identified as zona free must be handled with additional care.

Aim:
This is a case study of a 34 year old woman and her 34 year old male partner who presented with a history of failed fertilisation via standard IVF insemination and potential absence of ZP.
Three treatment cycles were undertaken at Monash IVF Gold Coast; ultimately resulting in a clinical pregnancy and anticipated live birth.

Method:
Ovarian stimulation via FSH+GnRH Antagonist and trans-vaginal oocyte retrieval led to collection of cumulus oocyte complexes (COCs).
COCs were prepared for ICSI using dilute hyalase solution. ICSI performed on all viable oocytes where determination of probable polar body was possible and subsequent culture in G-TL single step culture medium (Vitrolife) and EmbryoScope+ (Vitrolife).
Ultrasound guided transfer of a single blastocyst took place on day 5, remaining blastocyst vitrified and stored for future use.

Results:
24 apparent COCs collected. 14 x oocytes suitable for ICSI. 4 x displayed evidence of fertilisation (2PN). 2 x blastocysts formed, 1 x transferred on day 5, 1 x frozen.
Patient demonstrated positive hCG result and clinical pregnancy confirmed via ultrasound (singleton). Expected date of delivery 28/06/2019.

Conclusion:
A modified approach to oocyte retrieval, handling, ICSI and embryo culture can lead to successful creation of blastocysts in zona free patients.
Furthermore the utilisation of time lapse and single step media to provide uninterrupted culture and observation of developmental milestones was advantageous and yielded a positive outcome for this couple.

References:

Stanger, J.D., Stevenson, K., Lakmaker, A., Woolcott, R., (2001) Pregnancy following fertilization of zona-free, coronal cell intact human ova: Case Report, *Hum Reprod* 16(1): 164-167.

Rankin, T. and Dean, J. (1996) The molecular genetics of the zona pellucida: mouse mutations and infertility. *Hum. Reprod.* 2:889–894.

Providing Complementary Care for Complex Patients: The Intersection Between the Roles of Genetic Counsellors and Infertility Counsellors

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Background:
As genetic testing technologies become increasingly complex, so too does the *genetics* component of the genetic counsellor's role. For many patients and non-genetics colleagues, it can be easy to focus on the *genetics*, leaving little space for the *counselling* in a genetic counselling interaction.

Aim:
This presentation aims to highlight the *counselling* in genetic counselling, and explore the interplay between genetic counsellors and infertility counsellors in a clinic-based setting.

Method:
Using an in-depth case example, the author will illustrate the interwoven roles of genetic counselling and infertility counselling to provide supportive team based, patient centred care for couples with complex genetic and counselling issues.

Results:
For some patients, the role of the genetic counsellor is seen as quite separate and discrete from the role of the infertility counsellor. Situated in an IVF clinic setting, genetic counsellors may often be considered by patients as primarily useful for facilitating preimplantation genetic testing (PGT) prior to commencing IVF treatment, or understanding complex PGT results. Patients seeking counselling support during their IVF treatment may in fact do so from both genetic and infertility counsellors.

Conclusion:
Genetic counsellors are highly skilled allied health professionals with a unique skill set and a strong support and counselling focus, aimed at assisting individuals to understand and adapt to the complex implications of genetic information for their family. The care provided by genetic counsellors and infertility counsellors in a clinic-based team can meet complex needs in a complementary and supportive manner.

Antenatal Management of IVF Pregnancies

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Introduction:
Pregnancies conceived by in-vitro fertilisation (IVF) are at increased risk of adverse perinatal outcomes, including preterm birth, low birth weight and congenital anomalies[1]. Despite these risks, there is a paucity of guidance on the antenatal management of IVF pregnancies, and variation exists between clinicians. In the public hospital setting, there are various models of antenatal care available. This study was conducted to examine who manages IVF pregnancies antenatally in a public hospital, and to determine if any differences exist in patient outcomes.

Methods:
Data on all singleton IVF pregnancies managed at a principal referral public hospital in NSW between 2014 and 2018 was examined. Data was analysed from the Obstetrix and eMaternity databases.

Results:
There were 314 IVF pregnancies (2.3% of all pregnancies) who birthed in the 5 year period, with 335 live births and 1 stillbirth. 185 (59%) were managed through midwifery led antenatal care, 101 (32%) in an Obstetric led high-risk antenatal clinic, 27 (9%) were managed by a private Obstetrician, and 1 (0.3%) had no antenatal care. Women managed through the obstetric-led clinic were older (35.5 vs 33.2 years), had more preterm deliveries (16% vs 6%), delivered more low birthweight babies (18% vs 2%), had more caesarean sections (57% vs 23% of deliveries), and had a higher incidence of gestational diabetes (24% vs 8%).

Discussion:
Results indicate that IVF pregnancies are largely being managed in a midwifery care setting. Poor perinatal outcomes still occur amongst this lower-risk group, so development of a guideline for the antenatal management of IVF pregnancies may be beneficial for clinicians, both midwifery and medical.

References:

In vitro fertilisation: Perinatal risks and early childhood outcomes. Scientific Impact Paper No. 8, RCOG, May 2012

Follistatin-Like 3, an Activin a Binding Protein, is Involved in Early Pregnancy Loss

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Background:
Early pregnancy loss (EPL), a common and severe complication in pregnancy, has a long-term personal and social impact. Belonging to the transforming growth factor β (TGFβ) superfamily, the over-expressed activin A is found to be associated with pregnancy loss in women. Activin A increases follistatin-like 3(FSTL3) at both the mRNA and protein levels. In turn, FSTL3 binds activin A and prevents it from binding to its own receptors, thereby blocking the downstream signaling pathways of activin A. Thus, the negative feedback loop between the FSTL3 and activin A can protect cells from accepting excessive activin A. Furthermore, our previous study has evidenced that FSTL3 contributes to the invasion and migration of trophoblast which are critical for a successful pregnancy. This study aimed to identify the roles of FSTL3 in the establishment and maintenance of pregnancy, and to determine whether FSTL3 is involved in the pathophysiology of EPL.

Aim:
To clarify the roles of FSTL3 in the establishment and maintenance of pregnancy and the involvement in the pathophysiology of EPL.

Method:
Endometrial Ishikawa cells and JAR cells were cultured and FSTL3 siRNA was used to silence FSTL3.The embryo adhesion sphere experiment *in vitro* and the ICR mice model *in vivo* were used to investigate how the FSTL3 functioned in embryo adhesion and implantation respectively. The villus tissues of women with EPL and women with normal pregnancy were collected, and the western blotting was used to determine the expression of FSTL3 and activin A in the tissues.

Results:
FSTL3 siRNA greatly reduced FSTL3 expression($P<0.001$). In the *in vitro* study, silence of follistatin-like 3 in JAR cells significantly reduced the number of trophoblast spheroids adhered onto endometrial Ishikawa cells compared with scramble siRNA($P=0.0297$). For the *in vivo* system, the number of embryos implanted in the uterine horn injected with FSTL3 siRNA mixture was substantially less than that in uterine horn injected with scrambled siRNA ($P<0.001$).
There were no significant differences in either the maternal age ($P=0.1875$) or the gestational age ($P=0.4162$) between EPL women(n=20) and the controls(n=20). The expression of FSTL3 and activin A were significantly increased in the villus tissues of women with EPL compared with that of women with normal pregnancy.

Conclusion:
FSTL3 regulates embryo adhesion and embryo implantation. The expression of FSTL3 and activin A is markedly increased in villus tissues of women with early pregnancy loss. It suggests FSTL3 has biological roles in the establishment and maintenance of normal pregnancy and may play a protective role in pathophysiology of early pregnancy loss.

Novel Observation of Dispermic Fertilization of a Human Oocyte that Developed into a Zygote with Two Pronuclei and Two Polar Bodies Using High-Resolution Time-Lapse Cinematography

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Background:
We occasionally encounter miscarriages of polyploid identified by chromosome analysis even though normally-fertilized oocytes (2PN/2PB) were selected and transferred in IVF or ICSI treatments. These were supposed to be caused by the fertilization with non-haploid gamete or the failure of polar body (PB) extrusion by chromosome nondisjunction.

Aim:
We analyzed time-lapse images of an oocyte that was penetrated by two sperm to find out why two pronuclei, rather than three, were formed.

Method:
Since 2003, we have collected 235 oocytes donated from 220 patients and observed them in culture for 2 days using high-resolution time-lapse cinematography (hR-TLC). Digital images were acquired with an exposure time of 1/20 second. After hR-TLC observation, good-quality embryos were used in embryo transfer or cryopreserved for future clinical use.

Results:
We observed one case of dispermy. The sperm that penetrated the zona pellucida (ZP) most deeply (the leading sperm) was identified and brought into focus by the micromanipulator. The other sperm penetrated a different part of the ZP, almost as deeply as the leading sperm. 83.5 minutes after insemination, the leading sperm penetrated the ZP and bound to the surface of the oocyte close to the first polar body. 30 seconds later, the other sperm penetrated the ZP at an angle of 90° relative to the first PB. Although penetration of ZP by two sperms was confirmed visually, two pronuclei formed afterward. The resultant oocyte was multinucleated, cytoplasmic fragmentation was severe during the first cleavage, and became a poor-quality embryo.

Conclusion:
We observed a second sperm entering a human oocyte 30 seconds after the first sperm entered, creating a 2PN/2PB embryo. Although we did not confirm the polyploidy of this embryo, the phenomenon captured in this study could be one of the reasons of 2PN polyploids.

Is there a Place for Surgery for Endometriosis Before IVF?

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Background:
Endometriosis is a common condition affecting 8% of women. 1 in 20 babies in Australia are born to assisted reproductive technologies, and a significant portion of these women will have some degree of endometriosis.

Aim:
Literature review and update on endometriosis and surgery before IVF.

Method:
Presentation of existing guidelines and updates in the literature. Discussion of special situations and evidence surrounding these.