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Repromed

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9:05 - 9:30 Advances in Assisted Reproduction – What’s New?
Advances in Assisted Reproduction - What’s new?

Dr Guy Gudex
Medical Director
The beginning......

- 1973 world’s first human IVF biochemical pregnancy Melbourne
- 1976 world’s first clinical pregnancy (ectopic) announced by Steptoe and Edwards UK
- 1978 world’s first IVF baby born UK after 102 embryo transfers, 2nd baby Jan 1979 UK
- 1980 world’s 3rd IVF baby born Melbourne
- 1984 world’s first frozen embryo baby Melbourne
The beginning

1983 world’s first donor egg baby Australia
1985 - transvaginal oocyte retrieval published
1986 world’s first baby born from a frozen egg
1989 world’s first baby born following PGD (UK)
1992 world’s first baby born using ICSI in Belgium
1994 - world’s first IVM baby born
1998- world’s first IVF baby from GnRH antagonist
The beginning

1999 - world's first baby born from vitrified oocyte

2000 - world's first baby born from vitrified blastocyst

2009 - octuplets born in California - 12 thawed embryos transferred

2013 - cloning from nuclear transfer from human fibroblasts to enucleated oocytes. Planned to develop blastocysts to obtain embryonic stem cells
ICSI - A significant advance
ART in NZ

50% private funding, 50% public funding

Population based funding with access determined by CPAC threshold 65 points and exclusion criteria nationally

Scoring and referral for treatment can be through private or public FSA

Eligibility criteria vary region to region for public FSA - NRFS allows BMI over 32 and smoking
ART in NZ

Current wait time for public FSA 3-4 months

Current wait time for treatment average of 12 months - ART outside elective surgery guidelines

PGD funded separately, no funding for PGS

Private treatment expensive with no insurance cover - IVF/ICSI $12,000 including medications on average
ART in NZ - 2012 ACART Report

- 5,177 ART cycles
  5.9 cycles /1000 women aged 15-44

- 96% of cycles IVF 64%fresh - 32% thaw

- LBR 30% per fresh ET overall
  40.5 % under age 35

- Average age women 35.9y
  22% aged 40 or more

- SET rate - 70% fresh ET 91% thaw

- Multiple pregnancy rate 5.2%
Age and pregnancy rates

Live Birth Rate for Fresh Transfers by Woman’s Age

ANZARD 2013
AMH Profile

- >75% Percentile: Probable PCOS
- 25-75% Percentile: Normal Ovarian Reserve
- <25% Percentile: Low Ovarian Reserve

Graph showing AMH levels across different age groups.
Indian woman gives birth at 70 with help from IVF

The Telegraph

Feb 2016
Definitions....

Advanced maternal age (AMA) >35 yrs old

Very advanced maternal age (VAMA) >45 yrs old

Increasing numbers of women having first pregnancy at age >40 yrs
Issues:

- Maternal mortality - low but probably risk increased

- Maternal morbidity increased
  e.g. risk of hypertension 35% women 50y with egg donation pregnancy

- Still birth risk significantly increased in VAMA

- Ethical concerns - patient right to choose treatment vs clinical right to refuse access

- Appropriate screening
  ECG, HbA1C, physician review, mammography
Screening for heart disease pre ART

- History - family, smoking, hypertension, hyperlipidaemia
- Congenital heart disease
- Consider stress echocardiography (stress ECG 50% false positive)
- CT angiography if indicated (radiation with modern machine equivalent to 6-8 months background radiation)
Social Egg Freezing (SEF)

• Not an insurance policy against childlessness

• Average age in UK for SEF 38 years

• Alternative to sperm donation for single women

• Ideally done under the age of 35 years
So Eager for Grandchildren, They're Paying the Egg-Freezing Clinic
What’s being offered...

- Most clinics offering social egg freezing if requested, but do not promote it
- Success rates with oocyte vitrification probably equivalent to IVF but very age dependent
- Ave 15-20 oocytes required (2-3 cycles)
What should we be doing?

1. Try and better adapt to the needs of working and/or future mothers
2. Creating better public awareness about age related reproductive decline and fertility preservation
3. Offer age specific information and counselling - women in their 20’s and 30’s should be counselled about the age related risk of infertility when they present for sexual health or contraception discussion.
4. Offer predictive tests such as AMH
5. Try and convince those women who may benefit from SEF to present before the age of 35
OHSS Prevention

- AMH - threshold 35 pmol/l increased risk
- Metformin - 2014 Cochrane review found a reduction in OHSS risk and improvement in CPR with IVF
- Antagonist cycle - 50% reduction in severe OHSS
- Agonist trigger and freeze all
- Trials with Kisspeptin under way

However, the use of this insulin-sensitising agent increased clinical pregnancy rates and decreased the risk of OHSS.
Patient Friendly IVF

- Antagonist cycles significantly reduce treatment burden including side effects

- Milder stimulation with reduced dose FSH

- Depot FSH preparations- Elonva

- Oocyte retrieval simpler with LAS and taper needle
The efficiency of IVF depends mainly on 3 factors:
- Embryo status represented by its chromosomal complement
- Endometrial receptivity - might be improved by FET
- Embryo transfer technique

Current Challenges remain –
- To identify better selection methods for identifying embryos with higher implantation potential
- To improve and standardize IVF protocols & lab practices
Improving success rates in IVF
Antioxidants

• Cochrane Review Aug 2013 on oral antioxidants for **female** subfertility - no evidence of increase in CPR or miscarriage risk

• Cochrane Review Dec 2014 on **male** antioxidants for male subfertility- probable doubling of CPR with treatment

• ProConceptia, Menevit, Vitamenz

• Melatonin 3mg daily for women
Improving Implantation

EmbryoGlue for Embryo transfer medium

Hyaluronic Acid

Important macromolecule in the female reproductive tract at time of implantation

Cochrane meta-analysis of ~4000 patients shows significant improvement in Live birth rates
Improving Success Rates
EmbryoGen for Optimal Embryo Dialogue

Growth Factor – GM-CSF
Multi-centre trial 1400 patients show significantly more Live Births in women with repeat miscarriage & failure of IVF

Reported Actions:
• Enhanced embryo quality
• Facilitates dialogue between embryo and endometrium for improved implantation
Current Methods of Embryo Selection

Invasive
- Preimplantation Genetic Screening (Only method to screen for Aneuploidy)

Non-Invasive
- Embryo Morphology (primary / widely used)
- Time-Lapse kinetics
- Metabolomics
Aneuploidy - Why bother?

Dramatic decline in IVF success rates with maternal age is mainly caused by embryonic aneuploidy

(Hassold et al., 1996; Vialard et al., 2011)
Embryo Biopsy for PGS
EmbryoSelect @ Repromed

- Repromed now offers ‘EmbryoSelect’ which is Pre-implantation Genetic Screening (PGS) using Next Generation Sequencing (NGS)

- Identifies the most competent (euploid) embryos for transfer

- Indications for EmbryoSelect use in IVF include
  - Advanced maternal age (>35y)
  - Recurrent miscarriage
  - Repeated implantation failure
What’s the future?

- PGS offered to all women >35y undergoing IVF
- Blastocoelic fluid could be a potential source of DNA for PGS (ESHRE 2015)
- Technically feasible to extend NGS to allow whole genome sequencing of embryos

Opens up black box of ethical dilemmas and, regulatory framework should be in place to keep up with the pace of developments
Zika Virus and ART

• Increasing transmission including Fiji, Tonga and Samoa
• Can be transmitted through semen / intercourse
• Consider avoiding travel to affected countries
• Men and women returning from regions where Zika transmission occurs should wait 2 months before ART and 6 months if male partner symptomatic (rash, fever, myalgia, conjunctivitis)
• Consider freezing sperm prior to travel