ETHICAL CHALLENGES IN FERTILITY
RCOG – CAPE TOWN 2017

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DISCLAIMER

- This presentation has been prepared for medical and scientific interest. The content of the presentation expresses the views of the speaker and is based on their clinical experience and research material from various sources.

DISCLOSURE

- No conflict of interest to disclose.

TALK

- 1. FERTILITY IN THE **OLDER/PERI- OR POSTMENOPAUSAL WOMEN**
- 2. OOCYTE VITRIFICATION FOR **SOCIAL FREEZING** – ETHICAL LESSONS FOR PATIENT COUNSELLING
- 3. THE UNTOLD GRIEF OF **CHILDLESS MEN** – ETHICAL LESSONS LEARN
- Key points/ Summary

FERTILITY IN THE OLDER/PERI- OR POSTMENOPAUSAL WOMEN

INTRODUCTION 1

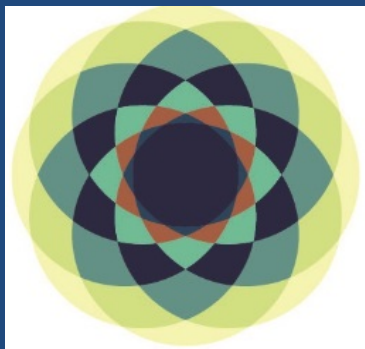
- Some interesting Australian data:
  - ± 3% of Australian births are from **ART**
  - ± 9% of Australian couples are experiencing **infertility**
  - Average age of women trying "**own eggs**" ART = 36yrs
  - Average age of women using **donor eggs** = 40.8 yrs
  - 25% of Australian ART is to assist women > 40 yrs
  - Only 1% of women > 44 yrs will deliver a **live baby**

INTRODUCTION 2

- **Oocyte donation** in RSA not as common as abroad
- **Requests** for donor oocytes in couples with younger male and peri-/post menopausal female **growing**
- **Challenges** in guiding these couples to make an informed and sound decision in their unique circumstances discussed in a few recent articles.
  - Grossman et al. Expert Rev. Obstet.Gynecol 2012
  - Ethics Committee of ASRM. Fertil.Steril 2016

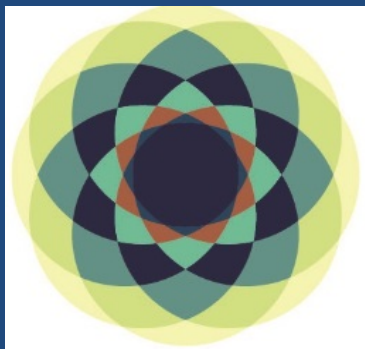
Success rates of oocyte donation in older women

- Success of donor oocyte IVF (D-IVF) in older pre/post menopausal women established in 1990's, however **concerns** about offering D-IVF to woman > 50yrs
  - Receptivity of normal menopausal uterus, even if hormonally prepared, for normal embryo development?
- Animal studies - ↓implantation with ↑maternal age
  - Harman et al. J Reprod. Fertil, 1970
  - Holinka et al. Biol. Reprod, 1979
- Human Studies (Pt's > 50yrs) proved **similar histology and implantation rates** when compared to younger woman
  - Sauer et al. J Am Med Assoc, 1992
  - Sauer et al. J Assist Reprod Genet, 1993



Success rate of oocyte donation in older women 2

- **10 yr review** of PM women at Univ of Southern California
  - Mean age 52.8 ± 2.9 yrs
  - 121 ET`s (89 fresh/ 32 frozen) D-IVF
  - PR = 45.5% and LBR = 37.2% ≈ younger Pts
    - Paulsen et al. JAMA, 2002
- **SUCCESS** of oocyte donation in women > 50 – 60yrs → pregnancy still possible in all woman with **NORMAL UTERUS** regardless of ovarian status and determined by **AGE OF DONOR**
    - Sauer et al. Lancet, 1993
    - Kort et al. Am J Perinatal, 2012
    - Paulsen et al. Fertil Steril, 1997
    - Antinori et al. Reprod Biomed Online, 2003



Maternal and foetal risks

- While D-IVF is successful in older women it does carry some **RISKS**
- **MATERNAL RISKS** (Advanced maternal age = AMA > 35 yrs)
  - ↑risks of preg related complications
    - Hpt disorders/Gest DM/abn placentation/prem deliveries/stillbirths/↑CS
      - Kirz et al. Am J Obstet Gynecol, 1985
      - Shrim et al. J Perinat Med, 2010

Maternal and fetal risks 2

- **FETAL RISKS** (AMA)
  - SGA/RDS/admission to NICU/↑overall mortal
    - Shrim et al. J Perinat Med, 2010
- Thus as maternal age increases above 50 yrs → ↑ factors contributing to maternal and neonatal morbidity/mortality
- GREATER **CONCERN**
  - Reports of **cardiac arrest** and **worsening HELLP syndrome** after twin delivery in D-IVF in older women
    - Schutte et al. Reprod Health, 2008
- THUS **MEDICAL SCREENING** advised

SCREENING RECOMMENDATIONS FOR WOMEN OVER THE AGE OF 50YRSPRIOR TO ATTEMPTING PREGNANCY

- **Medical** and **reproductive history** including general **physical** exam and **pelvic exam**
- **LAB TESTS**
  - Std preconception tests and counselling
  - Rubella + Varicella titres
  - FBC
  - Complete metabolic screen
  - Fasting lipid screen
  - TSH
  - Coagulation studies
  - Haemoglobin A1c or gluc tolerance test
  - Pap test incl N gonorrhoea + C trachomatis
  - Inf disease screen (HIV, Hep B + C)
  - Stool testing for occult blood

SCREENING RECOMMENDATIONS FOR WOMEN OVER 50 YRS PRIOR TO ATTEMPTING PREGNANCY 2

- **Imaging**
  - ECG or ECHO of heart (if abn stress test or ↑risk factors)
  - Mammogram
  - CXR
  - Transvaginal ultrasound
  - Assessment of uterine cavity (hysteroscopy)
  - Colonoscopy
  - Skin cancer survey
- **Mental health and Psychological assessment**
- **Optimization of health** – pre-conceptually involving **specialists** in Internal medicine/foetal medicine + guidance from a psychologist with interest in reproductive health

ADVANCED PATERNAL AGE

- Associated with:
  - **Chromosomal abnormalities** (Downs, Klinefelter, Autism, Schizophrenia etc.)
    - Fish et al. J Urol, 2003.
    - Lowe et al. Am J Hum Genet, 200[illegible]
    - McIntosh et al. Epidemiology, 1995
    - Reichenberg et al. Arch Gen Psychiatry, 2006
- Clinical data **difficult to evaluate** as maternal age often increases with that of the partner
- 2 smaller studies suggest fertilization, pregnancy, LBR and risks of **abnormalities** in male > 50yrs ≈ to offspring of younger males if D-IVF
    - Gallardo et al. Fertil Steril, 1996.
    - Paulsen et al. Am J Obstet Gynecol, 2001

MULTIPLE PREGNANCIES AND INCREASED RISKS

- **SET** (single embryo transfer), to limit multiple pregnancies in older patients, is essential in order to lessen complications.
- **ASRM guidelines** in regards to number of embryos transferred to recipients of DONOR oocytes is very useful.
    - Practice Committee of ASRM guidelines. Fertil.Steril, 2016
- **Transfer of >1 embryo** should be a decision taken after careful discussion between parents to be and the clinician.

What happens in practice?

- **SET?**
- Wijnland fertility (www.wijnlandfertility.co.za)
- New (ish) Technology (**Embryo scope**/Timelapse)
  - ↑PR/ET from 63% → **69%/ET** (>800 cycles)
  - ↑implantation rate/ embryo from 41% → 50%
  - ↓ number of embryos/ET from 1.98 →**1.15.**
  - ↓ multiple PR from 23% → **8%**

ETHICAL CONSIDERATIONS

- Should we have the **RIGHT to reproduce**?
- Ethical dilemma is the balancing of the interest of the patient's **AUTONOMY** for reproductive freedom and that of the **CHILD** born from a patient of advanced reproductive age
- Older parenthood raises a variety of important factual and **ethical questions –** consider patient **RIGHTS**, their physical and **MENTAL** well being
    - Caplan et al. Seminars in Reproductive Medicine, 2010
- Reproductive freedom/ imposes a double standard?
- There exists a **DOUBLE STANDARD** between men vs women
- Different kind of families and **CULTURES**: single/same sex and heterosexual older women (psychologist more concerned about **single mothers**, regardless of age)
- Dealing with two **LIFE CHANGING** stages of life for women: end of own reproductive stage of life vs "my own" infertility

ETHICAL CONSIDERATIONS

- Are you ever **TOO OLD** to have a baby? – is this the most important question?
- Safety/Economic/Psychosocial impact?
- Maria Bousada, 66yrs, single (Californian) mother died 3 yrs after conceiving with donor eggs leaving behind her 2 yr orphaned twins
- **AGE LIMITATIONS** to ART can be divided
  - Physiological reproductive age
  - Technical capabilities of ART
  - Social limitations

SOME MORE QUESTIONS ASKED

- How do we describe **OLDER parenting** and fertility treatment?
- Older parenting is in effect "a natural **EXPERIMENT**" in which a key factor is changed – in this case the **AGE** of parents. The effects can be measured across several generations. Babies born to those parents are different, as are the parents that raise them and even the grandparents, "who, after all, have to wait a lot longer, than they used to, for grandchildren!
- Is it **LEGAL and ETHICAL** to offer fertility treatment and ART to older and PM women?
- Should infertility **programmes discourage, tolerate or encourage** pregnancy in old age?
- OR: Should **ETHICAL programmes** try to discourage and constrain who it is that can bear a child in their later years?

WHY DO WOMEN OF LATER REPRODUCTIVE AGE WANT TO HAVE CHILDREN

- **MOTIVATIONS** VARY
  - Cohen et al. Indiana Univ Press, 1996
  - " Forty may be the NEW THIRTY?"
  - Egg DONATION makes this possible
  - Older couples will use techniques such as sperm, egg or embryo donation, but keep the fact a SECRET
- The fact that a certain procedure is technologically **possible** does make it **ethically** right!
- Older single women – "WHY did they not find Mr Right"?
  - SOCIAL **IMPACT** ??! – Red lights!!

WHY DO WOMEN OF LATER REPRODUCTIVE AGE WANT TO HAVE CHILDREN

- When is a women **"TOO OLD"** to have a child?
- Arguments for **AGE LIMITS** for treatment
  - **HEALTH RISKS** for older women
    - Discussed earlier
    - Limit D-IVF **< 55yrs** due to lack of safety data for mom/baby
  - **SOCIAL FACTORS** – long periods of emotional stress
    - Financial support systems (single mothers – screen socio-economics)
    - Social support systems
    - Why only pick on women?
    - They are at bigger risk, but **older fathers** are a risk of ↑ incidence of babies with genetic problems and diseases
      - Sloter et al. Fertil.Steril, 2004
  - **CHILD WELLBEING**
    - Children needs parenting until 15-16yrs **(psychosocial)**
    - Cap at **50 – 55yrs** for D-IVF should be considered?
    - Human Fertilization and Embryology Authority (HFEA) – Code of practice – not set an age limit BUT rather guidelines for child welfare/parental risk factors/genetic predispositions

SOCIAL FACTORS AND CHILD WELL-BEING

- Older and PM women – ↓ **LIFE EXPECTANCY**
- Children that lose their parents at a young age are more at risk for **stress/depression and drug abuse**.
- **PARENTAL LOSS** is one of the most stressful life events for children or adolescents
    - Froman et al , 2012
- **PARENTING** imposes physical and emotional **demands** – difficult to meet for older parents
- Socially, both parents and children may experience **isolation and STIGMA** from having significantly older parents.
- In RSA – **CULTURALLY** appropriate for children to look after, care and support their ageing parents. **Is that fair??**

SOCIAL FACTORS AND CHILD WELL-BEING

-But – **MORAL PANIC** is fuelled by overly narrow, historical and culturally blind conceptions of family and child-rearing responsibilities

- Not uncommon in many countries – children to be raised primarily by their **GRANDPARENTS**
- Africa; India; China – **CULTURE** differences

WHAT IS RIGHT?

- We need **more DATA**
- Physicians should carefully assess each prospective case and **INDIVIDUALIZE**
- **ASRM guidelines** can be used as recommendations
  - **Protecting** best interests of **CHILDREN**
    - Grossman et al. Expert Rev Obstet Gynecol, 2012
    - Ethics Committee of the ASRM. Fertil Steril, 2016

CASE STUDY 1

- Moslem/ single women
- 48 years old
- B.A. Degree, Arts Business
- Height 1.64/weight 56kg
- Have not found “Mr Right”
- Healthy/Menopausal
- Applied for donor-embryo/Moslem couple
- Complicated pregnancy
- Ethical aspects of Moslem culture

CASE STUDY 2 - MEDICAL

- After psychological screening
- Fully informed (medical risks) – Fit and Well
- Down regulated → 3BB embryo (SET)
- Normal 13 and 20 week scans
- Transferred to colleague at 16 weeks
- 32 weeks → severe PE → renal failure → delivered at 32 weeks (baby girl/ 2.1 kg/ NICU → did well)
- Mother → atonic uterus with PPH → relook laparotomy → B-Lynch suture/4U rbs/2U FFP's → DC on D4 PP and had good recovery!

CASE STUDY 2

- 40 yr G0P0 – primary infertility – 2 years
  - Amenorrhoea – 5/12
  - FSH = 40, 57, 55 IU/L
  - Thin EL, AMH < 0.05 ng/ml, no AFC
  - Donor ova
  - Twins (3.6 + 3.7 kg) @ 38 weeks
  - Uncomplicated recovery
  - HT after breast feeding stopped (after good discussion)

CASE STUDY 2 (cont)

- 1 yr PP
- Amenorrhea on HT
- Nausea + Vomiting
- Bhcg = +
- Singleton pregnancy
- 36 weeks now
- All well
- Parents delighted
- NB!! – don't get caught out!

CONCLUSION

- Women of AMA – comprehensive **medical screening**
- Med and Gestational risks should be discussed – **Physician** familiar with these risks
- D-IVF for woman **> 50 – 55yrs – discouraged**
- **SET** !!
- Prospective parents – counselled by **Psychologist**
- Honesty with older women if they want IVF with **own genetic material**, even if they have regular cycles (↓↓ LBR!)

OOCYTE VITRIFICATION FOR SOCIAL FREEZING: ETHICAL LESSONS FOR PATIENT COUNSELLING

SOCIAL FREEZING (1)

- Cobo et al. Fertil.Steril 2015
  - 137 women
  - Returned to use oocytes, vitrified for non-oncological reasons
  - 120 had no medical condition (social reasons!)
  - Largest series reported on

SOCIAL FREEZING (2)

- **RESULTS**
  - **8 – 10 M2 oocytes** needed for reasonable success if < 35 yrs
  - More **individualized** approach if > 35yrs
  - Combined outcome from several clinics
  - Just successful clinics reporting??
  - Be **centre specific** if reporting (ETHICS!)
    - ESHRE + ASRM (Task force on Ethics and Law)

SOCIAL FREEZING (3)

- **RESULTS (2)**
  - 63% (social freezing) → 37 – 39 yrs old
  - 5.8% (social freezing) → significantly younger probably due to external triggering event?
  - **Single women mostly wait** – hope for partner and to avoid burden of treatment?
  - SUGGEST social **freezing at younger age** due to poorer outcome if > 36 yrs

SOCIAL FREEZING (4)

- **RESULTS (3)**
  - Short average storage time of 2.2 – 2.4 yrs in both ages from 31-35 AND 36-40 yrs
  - **? Not first use fresh ART** (own reserves)
  - SHOULD THEY BE COUNSELLED DIFFERENTLY??

SOCIAL FREEZING (5)

- **DISCUSSION**
  - **Frozen ova first?**
    - ↓ aneuploidy-related risks
    - ↓ time to pregnancy
    - Avoiding additional fresh ART costs
    - ↑ cost effective if only ONE CHILD desired
    - Leaves less ova if more children planned (Pt older)

SOCIAL FREEZING (6)

- **DISCUSSION (2)**
  - If **more that one child** planned - suggested
  - FIRST → spontaneous conception (age!)
  - SECOND → fresh ART
  - THIRD → frozen ova (alternative to donor ova!)

SOCIAL FREEZING (7)

- Several studies reported
  - **Absence of partner** → main reason for social egg freezing
  - **Relational status** of woman that freeze ova for non-oncological reasons
    - 58% return with partner
    - 42% needs donor sperm
    - <50% of single women (at freezing) – returned as a couple (unable to find partner??)

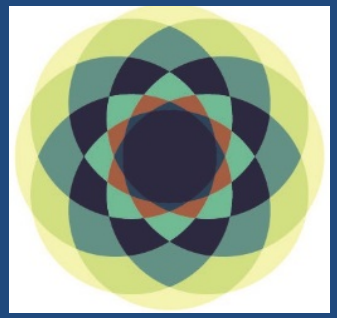
ETHICAL CONSIDERATIONS

- Reproductive “affirmative” action? (men vs women)
- Pre-birth genetic interventions (norm) – medical handicap (e.g.eyesight) parents’ fault??
- Obligation to freeze eggs – serious about career?
- Avoid self-blame
- Harm to women themselves? (harm to children?)
- Raising false hopes?
- Exploitation? (pt -> 40yrs)
- “Setting up” death of parent vs death of young parent?
- EGG BANKS ??

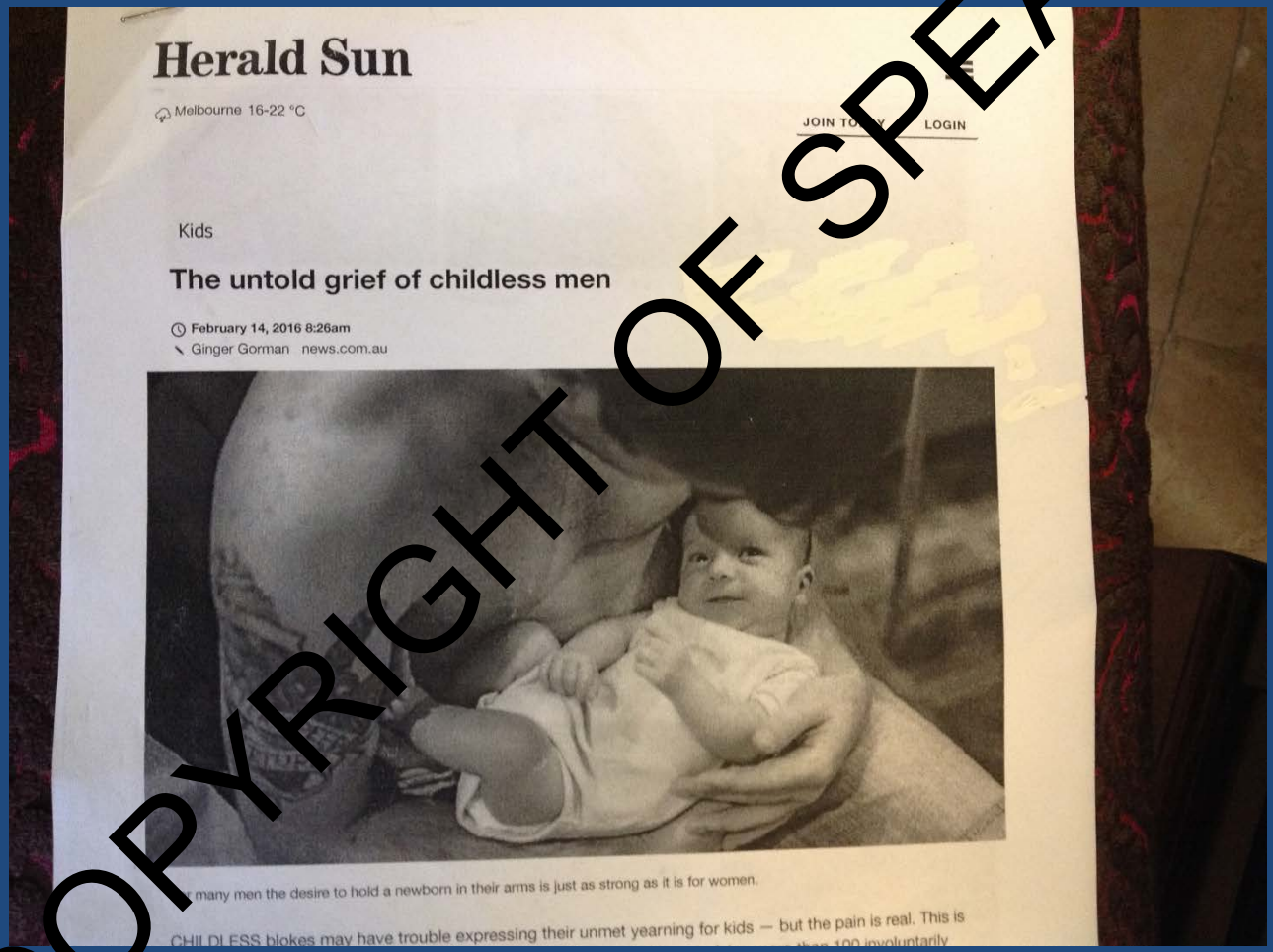
CONCLUSION

- Encourage egg freezing only when the procedure is most likely to succeed
    - Mertes et al. Reprod Biomed Online 2011
- Honour the principle of autonomy while insisting on better information about utilization and outcomes!

THANK YOU!



THE UNTOLD GRIEF OF CHILDLESS MEN: ETHICS AND LESSONS LEARNT



Herald Sun

Melbourne 16-22 °C

JOIN TO[illegible] LOGIN

Kids

The untold grief of childless men

February 14, 2016 8:26am

Ginger Gorman news.com.au

many men the desire to hold a newborn in their arms is just as strong as it is for women.

CHILDLESS blokes may have trouble expressing their unmet yearning for kids — but the pain is real. This is

CHILDLESS MEN (1)

- **HERALD SUN**
  - Melbourne – 14 Feb 2016
- Non scientific
- A few thoughts!
- A reality for many and unrecognized!

CHILDLESS MEN (2)

- Dr Robin Hadley
  - Hadley R et al. J Reprod Infant Psych, 2011.
  - British Sociologist
  - 100 involuntary childless men studied
  - 10 year study period

CHILDLESS MEN (3)

- Some strong phrases noted:
  - "it is an **unexpressed grief** – always with you"
  - " **black**" – frequently used to describe turmoil of facing a childless life
  - "a child gives you a **sense of the future**"
  - " if no child – a **legacy dies** with you!"
  - "outsiderness"

CHILDLESS MEN (4)

- Hadley et al. J Reprod. Infant Psych, 2011
  - Manchester University
  - 232 Pt interviewed
  - 59% men and 63% women desire to be parents
  - **Emotional impact** of childlessness men>women
  - Childless men **more angry/depressed** and felt more isolated than women counterparts
  - ↑ **risk** taking behaviour
  - Fear of being seen as "**paedophiles**" when in social situations with children
  - "fear of **loneliness**"

CHILDLESS MEN (5)

- MELBOURNE University research stats -2014
  - 530 000(13%) Australian men > 45 yrs are childless
  - 391 000 (9%) Australian women childless
  - Most men childless due to **circumstantial reasons**
  - (smaller number due to infertility)
  - If infertility – **grief twofold**
    - Failed IVF cycles
    - Childless
  - **Women get more emotional and physical support** from people around them, than men!

CHILDLESS MEN (6)

- **SOME GOOD NEWS**
  - If married and childless → can sometimes **make up the "loss"** by help shaping young lives
    - Teaching etc
  - some childless **couples become closer** if guided correctly
- THUS, WATCH OUT, GUIDE AND ALSO CARE FOR CHILDLESS MEN!
- Gender roll therapy suggested?
- **More research** needed

KEY POINTS/SUMMARY

- Women of AMA – comprehensive **medical screening**
- Med and Gestational risks should be discussed – **Physician** familiar with these risks
- D-IVF for woman **> 50 – 55yrs - discouraged**
- **SET** !!
- Prospective parents – counselled by **Psychologist**
- Honesty with older women if they want IVF with **own genetic material**, even if they have regular cycles (↓↓ LBR!)
- Social Freezing – understand the dynamics when counselling
- Men also important in their own journey!

THANK YOU

www.winlandfertility.co.za