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Fertility in focus

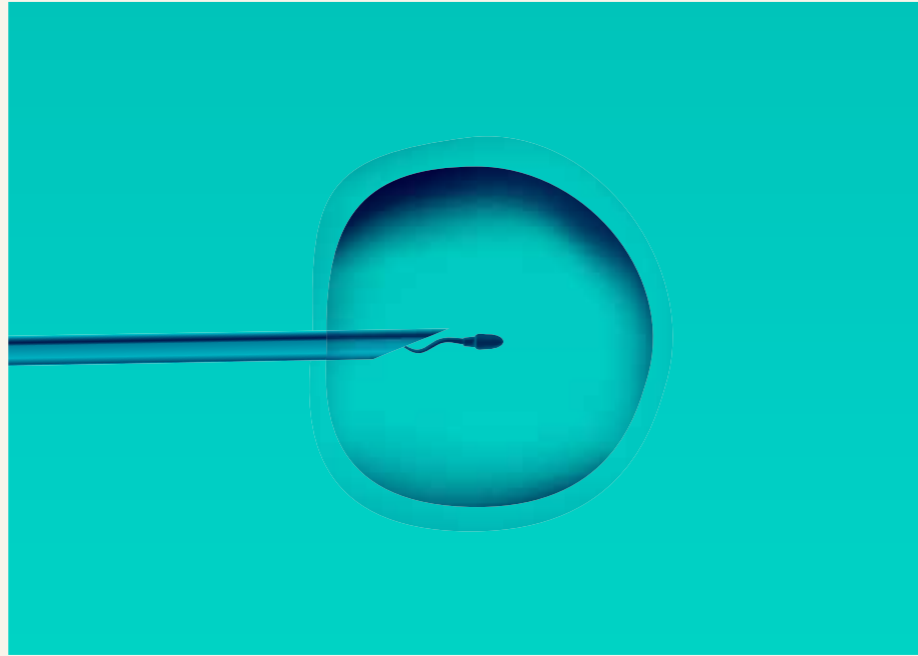


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Prof Luk Rombauts
PhD FRANZCOG MD CREI

Medical Director Monash IVF Group.
President-elect of the World
Endometriosis Society.
President of the Fertility Society of
Australia and New Zealand.



The Latest in Reproductive Care

Welcome to another issue of Monash IVF's Fertility in Focus newsletter. We are pleased to share with you the latest developments and updates in reproductive medicine which underpin our commitment to providing the best possible outcomes for patients on their fertility journey. This issue will cover a range of topics including fertility preservation, key considerations for genetic carrier screening, caring for patients with recurrent miscarriage and much more.

One of our most exciting developments in recent weeks has been the attribution of a \$15 million grant to help establish a five-year clinical trial of mitochondrial donation or 'three person IVF' in collaboration with Monash University. This incredible breakthrough positions us at the cutting edge of reproductive technology as an Australian-first and the world's second clinical trial of mitochondrial donation.

Every week in Australia, it's estimated one child is born with a severe form of mitochondrial disease, which can lead to premature death or a lifetime of debilitating illness and disability. By introducing mitochondrial donation, we can prevent some children from suffering life-threatening diseases and reduce the burden of mitochondrial disease on families and our health care system.

The aim of mitochondrial donation is to ensure only healthy mitochondria, the powerhouses of our cells that are vital to our survival, are passed on to an embryo by minimising the risk of prospective mothers passing on devastating mitochondrial disease to their children.

Used in conjunction with in-vitro fertilisation (IVF), mitochondrial donation techniques allow an embryo to be created which contains the:

- nuclear DNA from a man and a woman (the egg and sperm providers)
- mitochondria in an egg donated by another woman (the mitochondrial donor)

The awarding of the MRFF grant to the Melbourne researchers comes almost a year after the Mitochondrial Donation Law Reform Bill (Maeve's Law) passed Federal Parliament. In line with the Act, mitochondrial donation techniques will initially be legalised for research and training purposes.

Impacted families will be given access to the technology through a clinical trial to be funded by the MRFF grant. The research project's findings could then pave the way for mitochondrial donation to become more widely available through clinical practice.

Monash IVF is delighted to be a collaborator on such an important research project that has the potential to change the lives of many Australian families.

In addition to our continued dedication to research, we have also expanded our service footprint to enable more people to access fertility care across Australia. We have recently opened new purpose-built clinics in Albury (NSW), Penrith (NSW), Brisbane (QLD), Gold Coast (QLD - opening July 2023), Darwin (NT) and Cremorne (VIC). These expansions are fundamental in providing patient focused care in line with the increase in demand for treatments, including egg freezing, donor services and solo parents by choice. Our clinics aim to integrate best-practice science, technology and equipment, and are aligned to our ongoing commitment to providing patient-focused care to all people on their journey to parenthood.

As trusted partners in patient care, we hope you enjoy our latest update and we look forward to continuing to work together to help more people achieve their fertility goals.

While age and pre-existing conditions are two of the biggest factors impacting fertility, professional athletes can also face unique fertility challenges due to the impact high-performance sports training and competition can have on their bodies.

Monash IVF have formed a partnership with the Australian Athletes' Alliance (AAA), a professional body representing player and athlete associations including in AFL, cricket, football, basketball, netball, rugby league and hockey. The partnership aims to educate and empower sports stars to help them take early steps to optimise their reproductive health and give them the best chance of starting families when they are ready to.

Want to refer a highly active person who may be experiencing menstrual health or fertility issues?

E. info@monashivf.com

T. 1800 628 533



Fertility Wellness Partner





Dr Joseph Jabbour
MBBS FRANZCOG

Specialist Obstetrician, Gynaecologist and Fertility Specialist.

What is the Egg Freezing Process?

In recent times, there has been increasing demand for egg freezing, as it allows people with ovaries control over their reproductive life. Whether patients wish to delay pregnancy in pursuit of their career, a suitable partner, financial circumstances or due to health issues, egg freezing is a safe and financially viable option for fertility preservation.

Patients are assessed by a fertility specialist with initial workup involving screening blood tests such as serology for various infections, thyroid function tests, blood type and antibody screen, and Anti Mullerian Hormone level to estimate egg reserve. Pelvic ultrasound is performed to assess uterine morphology, endometrial thickness and to exclude obstructive lesions including polyps or synechiae. Ovarian volume and antral follicle count are also documented. Based on these results and the patient's age, a detailed and personalised 3-step egg freezing cycle is formulated.



“Whether patients wish to delay pregnancy in pursuit of their career, a suitable partner, financial circumstances or due to health issues, egg freezing is a safe and financially viable option for fertility preservation.”

Step 1 — **Hormonal stimulation**

This process usually takes anywhere from 10 to 12 days. The goal of controlled ovarian stimulation is to stimulate development of multiple ovarian follicles, after which multiple mature oocytes will be retrieved for cryopreservation. The first medication utilised is the daily administered FSH injection which stimulates the ovaries in a controlled manner to produce follicles.

Expected side effects of FSH treatment are minor and include bloating, with no limitation on normal day-to-day activities including work. Typically, on the 5th day a GnRH antagonist injection is administered daily to prevent spontaneous premature ovulation. These injections are self-administered under the close guidance and instruction of the fertility nurses at Monash IVF, including the timing of various injections and when to obtain pelvic scans and blood tests. Transvaginal ultrasound scans are utilised to quantify follicle number and size. Once the follicles reach a suitable size, the patient will be prescribed a trigger injection for ovulation, typically Ovidrel. Of note, with the more widely used antagonist protocols, the fertility specialist can elect to use a GnRH agonist to trigger final follicle development to reduce the risk of ovarian hyperstimulation syndrome.

Step 2 — **Surgical egg retrieval**

The egg retrieval procedure takes place 34-36 hours after trigger administration. The egg collection takes place in an operating theatre under general anaesthesia or with light sedation. This is a low-risk procedure where the eggs are collected from the follicles transvaginally with ultrasound guidance. A fine needle enters the pelvis through the vagina into the ovary, and gentle suction is applied to aspirate the fluid content of the follicles. Microscopy assessment is then performed intraoperatively by the attending embryologist to confirm the presence of oocytes within the sample. Ideally, each follicle will contain an egg. The patient is discharged home after 1-2 hours in recovery with prescribed rest for the remainder of the day. Procedural complications may include infection, bleeding, and rarely, injury to organs adjacent to the ovaries (<1:100).

Step 3 — **Freezing the eggs**

Upon arrival at the laboratory, a Monash IVF embryologist assesses the eggs for their maturity and the mature eggs will be selected for vitrification. This is a rapid freezing process that ensures fluids are extracted from the eggs to prevent damage by potential ice crystal formation. Once the eggs are vitrified, they can be stored for many years.

Reproductive aging is primarily related to the age of the patient when their oocytes are retrieved. The decline in fertility results from the decline in egg quality with increasing age as well as a reduction in egg reserve. Therefore, it is imperative to inform patients of their options to preserve their fertility with oocyte cryopreservation at a relatively young age.



Dr Tristan Hardy
MBBS (Hons) MRMed PhD
FRANZCOG FRCPA

Medical Director Genetics,
Monash IVF Group.

Top 10 Reasons to Consider Genetic Carrier Screening

1. Genetic conditions affect one in four hundred babies.

One in 400 babies that are born are affected by a genetic condition. Some genetic conditions are manageable, but others can have more serious outcomes. Patients who are able to identify potential genetic risks can work through their options by knowing their carrier status before conceiving.

2. Genetic carrier screening allows patients to understand their options earlier.

Undergoing genetic carrier screening before pregnancy gives patients time to understand their reproductive options without a time restriction. If patients find out that they have an increased risk of having a child with a single gene condition, having time to talk to a fertility clinician or genetic counsellor is incredibly valuable.

3. One in 20 reproductive couples will find out they have a high chance of having a child with a single gene condition.

Of the reproductive couples that undergo genetic carrier screening, one in 20 will discover they have a high chance of having a child with a single gene condition. In this situation, for every pregnancy there is a one in four chance of having a child with the condition they have screened positive for.

4. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists recommends genetic carrier screening.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) is the leading body for Obstetricians and Gynaecologists in Australia and New Zealand. They recommend that anyone considering pregnancy should be offered genetic carrier screening.

5. The majority of children born with a single gene condition have no other affected family members.

Patients may not know whether someone in their family has a single gene condition – but that doesn't mean that their children won't inherit a single gene condition from them. Genetic carrier screening will give vital information to patients to enable them make informed decisions about their reproductive options.

6. Patients can now complete genetic carrier screening at home.

Monash IVF now offers At-Home Genetic Carrier Screening Tests. Tests can be ordered online and are shipped directly to your patient's home. Patients don't need to come into a clinic for any procedures or tests – the test is completed in the comfort of their own home using a saliva swab.

7. Genetic carrier screening is easy and non-invasive.

Monash IVF's At-Home Genetic Carrier Screening Test just requires a saliva sample using the swab included in the kit and return via post. There are no needles or invasive procedures involved.

8. We're all carriers of around three to five genetic conditions.

On average, we're all carriers of around three to five genetic conditions. Most patients aren't aware of this, and most of the time being a carrier doesn't necessarily impact their health. About seven out of ten people having genetic carrier screening with us will find out they're a carrier of a single gene condition. Genetic carrier screening allows patients to understand the single gene conditions they carry and may pass on to any future children.

9. Genetic carrier screening can be done at any time.

Even if your patient is already pregnant, they can still undergo genetic carrier screening.

It is important to understand that it is different from non-invasive prenatal testing (NIPT), which assesses the chance of having a chromosome condition during each pregnancy. If your patient is not yet pregnant and find out they're a carrier of a single gene condition after completing genetic carrier screening, IVF and genetic testing of embryos may be one of the options offered to them.

10. Monash IVF's genetics team and clinical team are here to support your patients.

We understand that genetic carrier screening can raise a lot of questions and concerns. It's important to us that you're supported each step of the way.

That's why Monash IVF's At-Home Genetic Carrier Screening Test, comes with the support of our genetics team, including genetic pathologists and genetic counsellors. They can answer questions and help to understand what test results mean, and what patients's reproductive options are. We also have a team of fertility clinicians who can help patients conceive if they find out they're a carrier of a single gene condition. Our genetics team are lead by our Medical Director of Genetics, Dr Tristan Hardy, who is Australia's only Fertility Specialist, Gynaecologist and Obstetrician who is dually trained as a Genetic Pathologist.



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Your patients are not alone, we're here to help them every step on the way.

To order a kit scan this QR code or visit monashivf.com/genetic-testing

E geneticsadmin@monashivf.com
T 1800 684 198 (freecall)
monashivf.com

“It’s one of the most comprehensive tests on the market – we screen for 410 genetic conditions.”



Why you should refer a patient to Monash IVF for Genetic Carrier Screening

Your patient and their partner or donor will learn important information about their genetics, which can help them make informed decisions about their options for conceiving.

It's one of the most comprehensive tests on the market – we screen for 410 genetic conditions, and about 1 in 20 reproductive couples who have genetic carrier screening will find out they have an increased chance of having a child with a single gene condition.

You don't need to do anything - our expert genetic counselling team and fertility clinicians are on hand to support the patient every step of the way. If genetic carrier screening reveals that your patient has an increased chance of having a child with a single gene condition, our genetics team will provide them with support and personalised advice about their options.

If your patient does end up needing to test embryos in IVF or find a gamete donor, we're here to help them. We provide comprehensive fertility services, including IVF, preimplantation genetic testing of embryos, donor services and non-invasive prenatal testing (NIPT).



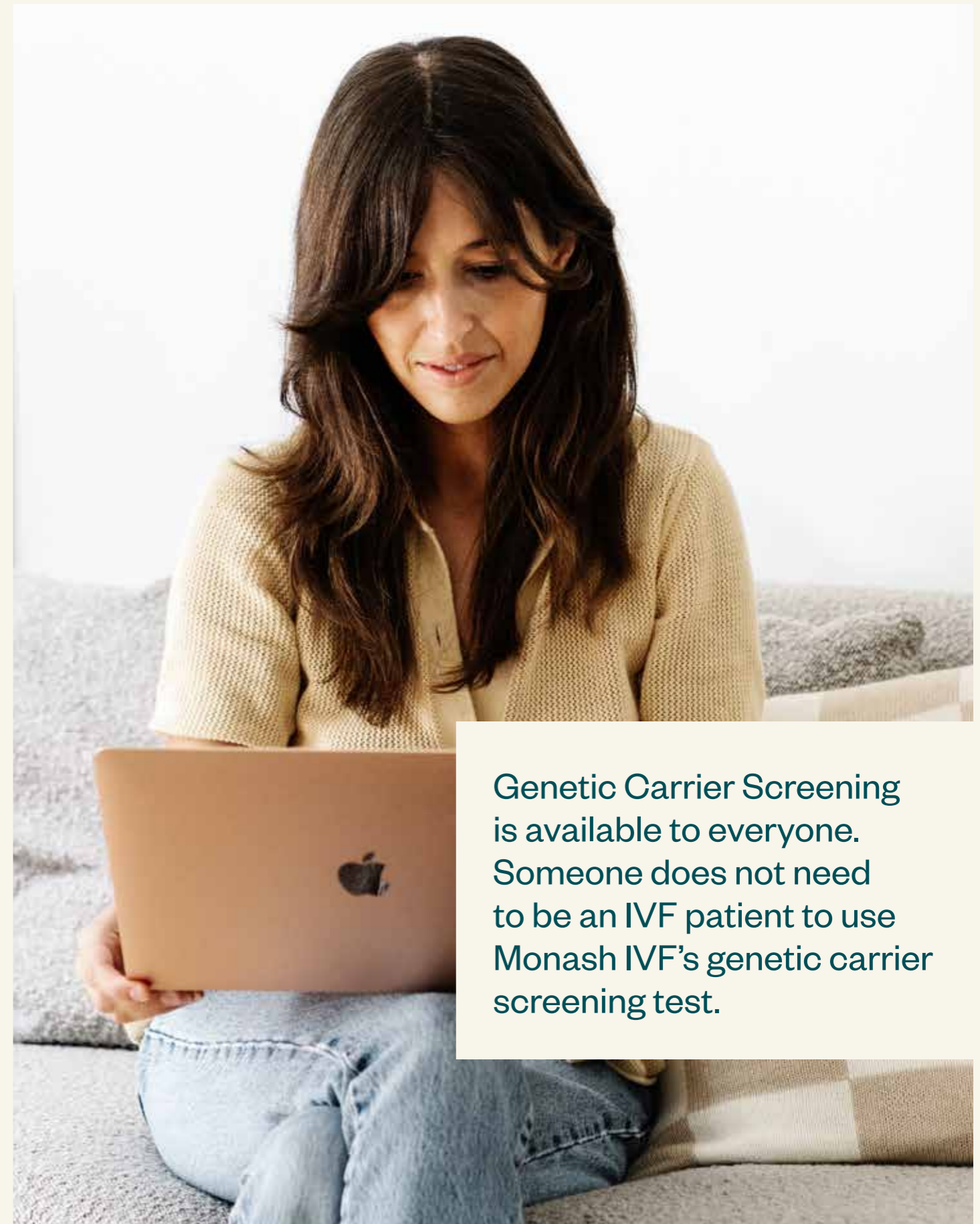
Should your patient want to do a genetics test in a clinic, please contact:

Sydney Ultrasound For Women
(for NSW patients)

T 1300 557 226
sufw.com.au

Melbourne Ultrasound For Women
(for VIC patients)

monashultrasound.com.au



Genetic Carrier Screening is available to everyone. Someone does not need to be an IVF patient to use Monash IVF's genetic carrier screening test.

“Many couples will be keen for investigations after a second miscarriage. For any couple that become pregnant again, TLC and monitoring of viability with weekly ultrasounds is equally important.”



Dr Vanessa King
MBBS FRANZCOG
MRMed

Obstetrician,
Gynaecologist and
Fertility Specialist.

Managing Recurrent Pregnancy Loss

Couples who experience consecutive miscarriage require empathy during this distressing time. Frustration is also often prominent as in at least 50% of cases there is no clear underlying pathology. Desperation can lead to investigations and interventions that have no proven benefit and there are few evidence based treatment strategies. Couples main concern is finding a cause and their risk of recurrence. This article concentrates on the proven investigations and management. Investigations can be commenced prior to referral to a specialist unit or fertility specialist/gynaecologist.

The definition varies between 2 or 3 losses and whether the pregnancy was biochemical or clinical. Many couples will be keen for investigations after a second miscarriage as the prospect of facing a potential subsequent miscarriage is daunting.

For any couple that become pregnant again TLC (tender loving care) and monitoring of viability with weekly ultrasound is equally important.



For management of recurrent miscarriage or fertility concerns:

Dr King is based in Fitzroy, VIC.

Contact directly on **03 9415 6077**

Causes and Potential Treatment

Chromosomal

Maternal age

The risk of miscarriage is strongly influenced by female age due to increasing aneuploidy rate and consequently the chance of recurrent miscarriage is also increased. The background rate of 3 miscarriages < 25 yrs is 0.13% but rises to 13% for those > 40 yrs.

Parental Structural Chromosome Abnormalities

These can account for 3-5% of cases and are mainly due to balanced translocations.

Genetic counselling may be required and discussion around the option of IVF with PGT for aneuploidy or translocations. For aneuploidy the outcomes are similar to expectant management but the number of miscarriages prior to a successful birth can be reduced.

Antiphospholipid Syndrome

This accounts for 5-20% of recurrent miscarriage and is a treatable cause. Positive Lupus Anticoagulant and Anti-cardiolipin antibodies 6 weeks apart are required for diagnosis. Haemtologist review is recommended. Treatment involves low dose aspirin prepregnancy and LMWH once pregnancy occurs.

Uterine structural abnormalities

The frequency of structural uterine abnormalities is increased in recurrent miscarriage and warrants investigation but their role in causation can be unclear. Uterine septum is the most common congenital abnormality (others include bicornuate, unicornuate and didelphys) and acquired pathology including fibroids and polyps. Pelvic Ultrasound in expert hands is needed for investigation. Uterine polyps should be removed and surgical management of uterine septum or submucous fibroids can be considered.

Endocrine

Hypothyroidism

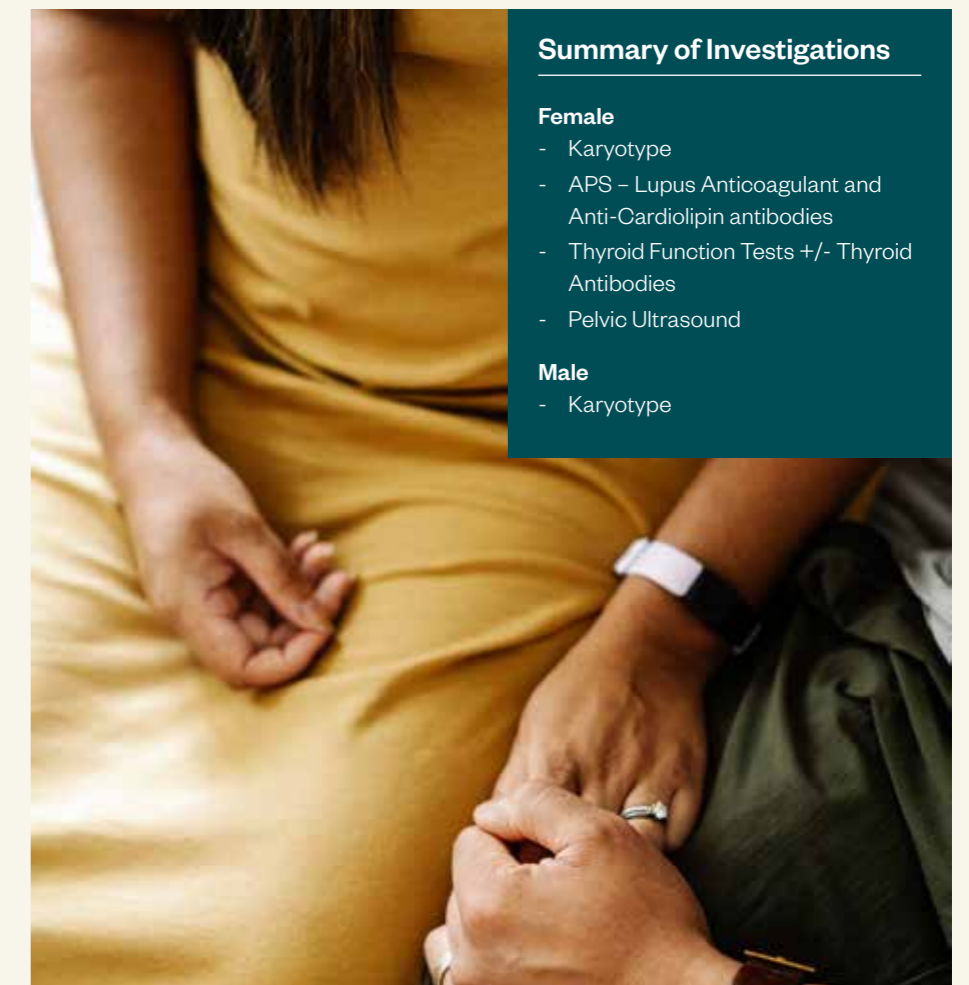
Overt hypothyroidism is a known cause but subclinical disease is less clear. Treating TSH levels over 4 mIU/L with thyroxine, especially when associated thyroid antibodies can improve outcomes.

PCOS

The miscarriage risk in PCOS is higher although the mechanism is unknown and a meta-analysis found that metformin did not reduce the miscarriage risk in PCOS.

Unexplained

For half of couples investigated no cause is found which can be both reassuring and frustrating. They can be reassured that the chance of live birth is still good. Lifestyle modifications should be encouraged especially to reduce smoking and BMI for obese women. Supplemental vaginal progesterone in the luteal phase has not been shown to improve the live birth rate but can be considered especially if there is bleeding in early pregnancy.



Summary of Investigations

Female

- Karyotype
- APS – Lupus Anticoagulant and Anti-Cardiolipin antibodies
- Thyroid Function Tests +/- Thyroid Antibodies
- Pelvic Ultrasound

Male

- Karyotype



Associate Professor David Shaker
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MMEd (Dundee)

Clinical Director - Monash IVF
Rockhampton and Townsville.
Specialist Obstetrician, Gynaecologist
and Fertility Specialist.

Stop the Clock Ticking

The biological clock impacts all aspects of human physiology, but it is nowhere more apparent than in female reproduction. While Assisted Reproductive Technology (ART) is advancing to overcome many of the causes of subfertility, the biggest challenge is to stop the clock ticking for the depletion of oocytes available for fertilisation.

Cryopreservation, utilising subzero temperature, has been tried for preserving semen from as early as the 19th century. However, the first report of human birth using cryopreserved semen was published only in 1954⁽¹⁾. Furthermore, it took almost 30 years to achieve a successful pregnancy utilising a frozen embryo at Monash University Australia⁽²⁾. Even then, successful oocyte cryopreservation was a dream. Even after the publication of the first report of pregnancy using a cryopreserved oocyte in 1986⁽³⁾, egg freezing continued to be an experimental technology. In 2013, the American Society for Reproductive Medicine removed the experimental status⁽⁴⁾, and egg freezing became part of the assisted reproductive practice.

Challenges of egg freezing

The challenges faced by egg freezing are caused by unique features of the oocyte, rendering it more susceptible to chilling injury than many other cells.

The oocyte has one of the most significant volume /surface area ratios between human body cells, which presents a challenge in achieving osmotic equilibrium with extracellular cryoprotectants.

Considering an oocyte is a cell in a mitotic division state, it is vulnerable to the damaging effect of freezing on the spindle. In addition, freezing stimulates the process of zona pellucida hardening, limiting sperm penetration.

Advances in cryopreservation techniques, especially cryoprotectants and rapid freezing as in vitrification, have overcome many of these vulnerabilities. In addition, using Intracytoplasmic sperm injection (ICSI) instead of standard IVF helped to overcome the challenge of zonal hardening.



How effective is egg freezing?

Studies showed many women who undergo egg freezing would not return for IVF utilising the frozen eggs⁽⁵⁾, which limits available data for frozen egg utilisation outcomes.

Studies comparing results of IVF using warmed cryopreserved eggs and fresh eggs reported a slightly smaller number of frozen eggs suitable for insemination but comparable fertilisation rate, pregnancy rate, and live birth rate⁽⁶⁾.

How safe is egg freezing?

Advances in medical technology are not assessed only for effectiveness but, perhaps more importantly, for safety, and egg freezing is no exception.

The safety of egg freezing programs for fertility preservation should consider two aspects. Firstly, the impact of oocyte cryopreservation on offspring, and secondly, the effect of stimulation protocols on women undergoing egg freezing before cancer treatment.

Data regarding the safety of the offspring resulting from IVF using frozen eggs is limited; however, a review of live-born babies after oocyte cryopreservation between 1986-2008 showed the rate of congenital abnormalities is comparable to the general population⁽⁷⁾. In addition, another study showed no difference in the percentage of aneuploid embryos on pre-implantation genetic testing between embryos formed using cryopreserved eggs or fresh eggs⁽⁸⁾.

Finally, ovarian stimulation protocols for egg collection are associated with supra-physiologic oestrogen levels, raising concern about the effect on hormone-sensitive tumours. The use of letrozole as an aromatase inhibitor is recommended to limit the rise of Oestradiol. The limited available data suggests that using these protocols does not cause marked short-term deterioration in breast cancer⁽⁹⁾.

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Conclusions

Thanks to advanced cryopreservation technology, egg freezing is part of the current practice of ART. Women desiring fertility preservation should be advised that while current data is limited, it suggests egg freezing is a safe and effective tool for fertility preservation.

“Research tells us that of the couples struggling to fall pregnant, approximately 30% will be due to problems with sperm function⁽¹⁾”



Dr Giselle Crawford
BMed (Hons.) MRMed FRANZCOG
Gynaecologist and Fertility Specialist.



Patients requiring a specialised Semen Analysis can contact Monash IVF.

Monash IVF have experienced andrology scientists at NATA accredited andrology laboratories at all major Monash IVF locations.

Contact us for a semen analysis referral kit at info@monashivf.com

Reference:

Newman J, Paul R, Chambers G. Assisted reproduction technology in Australia and New Zealand 2020. National Perinatal Epidemiology and Statistics Unit (NPESU), the University of New South Wales Sydney, 2022.

Severe Azoospermia: Options for Reproduction

Types of Azoospermia

Obstructive Azoospermia (OA)

Due to a blockage, can be caused by prior surgery, congenital abnormalities or previous infections.

Non-obstructive Azoospermia (NOA)

More commonly now referred to as Azoospermia due to spermatogenic defect (ASD). This is due to an issue with sperm production, can be caused various factors such as hormones, genetics, medical conditions. This is further categorised into primary causes (at the testicular level) or secondary (such as at the hypothalamic-pituitary level).

Possible Indicators of Azoospermia

- Klinefelters Syndrome
- Cystic Fibrosis
- Prior vasectomy
- Prior oncological treatment, such as radiation and/or chemotherapy
- Exogenous steroid hormone use

Determining a man's fertility

The most effective way to assess a man's fertility is via a Semen analysis. Semen analysis is also the most common base for all other laboratory male testing and is used to assess the concentration, motility and morphology of sperm.

If a semen analysis returns with no sperm?

You may wish to refer to a Fertility Specialist, Andrologist or Urologist at this point, who specialise in male infertility.

The initial recommendation is to repeat the semen analysis. This is best done in an andrology laboratory, with an extended search protocol.

Further investigations are recommended to further identify the aetiology, such as genetic testing, hormonal profile and testicular ultrasound. Other tests, such as tests for retrograde ejaculation may also be indicated.

If we are looking for sperm for the aim of ICSI, it may be recommended to proceed to surgical sperm retrieval.

A specialised Monash IVF clinician can offer the following options

Testicular Sperm Aspiration (TESA)

A needle is inserted into the testicle, and suction is applied to withdraw a small sample of testicular tissue. Any sperm can be isolated under a microscope. This is more commonly performed in cases of OA.

Testicular Sperm Extraction (TESE)

A surgical procedure whereby a piece of testicular tissue is removed via the scrotum. Any sperm can be isolated under a microscope. This is not frequently performed anymore due to the improved outcomes with MicroTESE.

Microdissection Testicular Sperm Extraction (microTESE)

This is a specialised micro-surgical technique used to retrieve sperm from the testicles of men with non-obstructive azoospermia. This is the gold standard approach to retrieval of sperm in NOA.

Expected recovery from surgical sperm retrieval

- Mild to moderate discomfort, recommend firm supportive underwear
- Icepacks to reduce swelling
- Analgesia, as required
- Usually performed as a day surgery procedure.
- Expect to return to normal activities after 2-7 days

Management of azoospermia, including MicroTESE, is available at Monash IVF Sydney OBD clinic with Dr Giselle Crawford.

Victoria

Monash IVF Cremorne

Level 1, 510 Church St
Cremorne 3121
T: 03 9420 8200

Monash IVF Clayton

Monash Surgical Private
Hospital Suite 1
252-256 Clayton Rd
Clayton 3168
T: 03 9590 8300

Monash IVF Hawthorn

Epworth Hawthorn
50 Burwood Rd
Hawthorn 3122
T: 03 9429 9188

Monash IVF Sunshine

Sunshine Private
Ground Floor, Suite 1
147 Furlong Rd
St Albans 3021
T: 03 9420 8292

Monash IVF Bendigo

Bendigo Day Surgery
1 Chum St
Bendigo 3550
T: 03 9590 8300

Monash IVF Geelong

Geelong Private
Medical Centre Level 2,
73-79 Little Rynie St
Geelong 3220
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Monash IVF Sale

Central Gippsland
Health Service
155 Guthridge Pde
Sale 3850
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Monash IVF Mildura

190-192 Ontario Avenue
Mildura 3500
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New South Wales

Monash IVF

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Level 10, 207 Kent St
Sydney 2000
T: 02 9154 1130

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Monash IVF Parramatta

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Monash IVF Penrith

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Kingswood 2747
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