REPROMED
REPRODUCTIVE UPDATE

Fertility in focus

GENETICS

SPRING
2024

Welcome

Welcome to our most recent edition of Fertility in Focus! Our primary goal with this newsletter is to provide you with the most recent advancements in science, technology, and specialised services available at Repromed. In this issue, I've decided to shift our attention towards genetics, particularly its role in fertility.

Bob Edwards, who won the Nobel Prize for his ground-breaking work in the development of In Vitro Fertilisation (IVF), thought that the aim of IVF in the future would be to provide new reproductive options for families with genetic conditions. More than 50 years after the first IVF pregnancy the Monash IVF Group (of which Repromed is a proud member), remains committed to this vision and harnessing the advancements in genetic technologies to provide world class, personalised fertility care to our patients.

From pre-conception carrier screening, through to pre-implantation genetic testing and non-invasive prenatal screening in pregnancy, our patients have access to the latest technologies and comprehensive genetic counselling services to support their unique needs whether they are seeking treatment as individuals or couples.

This issue of Fertility in Focus introduces some of the developments behind the scenes that are making this possible. If you have any questions or ever want to reach out to our team to see how we can help your patients or clinic, please contact us either at **enquiries@repromed.com.au** or **geneticsadmin@monashivf.com**. We here to help.

I would also like to draw your attention to our next Reproductive Health Summit on 26 October 2024 in Adelaide. Further details are on page 10. I hope to see you there as it will no doubt be another engaging and informative Summit!

Dr Juliette Koch
MBBS, FRANZCOG, CREI, MRepM

Medical Director - Repromed

Introducing our GP Portal

Fertility care resource hub

We are pleased to provide a range of resources for healthcare providers.

We also offer ongoing education regarding reproductive care options for both you and your patients. Resources for your clinic are also available upon request.

repromed.com.au/resources

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On-demand Medical Webinars

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Healthcare Professionals

"All individuals planning a pregnancy or in the early stages of pregnancy should consider genetic carrier screening."

Dr Juliette Koch
Medical Director - Repromed

Your Guide to Genetic Carrier Screening: Knowledge is Power

Genetic Carrier Screening is an important part of pre-conception and pregnancy care. In fact, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists recommend that all individuals planning a pregnancy or in the early stages of pregnancy consider genetic carrier screening. With the recent introduction of Medicare funding for "three gene" carrier screening, there is an increased need for information for prospective parents or those who are currently pregnant.

What does it test for?

With Genetic Carrier Screening, we can assess a patient's chance of having a child with a single gene condition. Single gene conditions occur when both biological parents are a carrier of the same genetic mutation (autosomal recessive conditions), or a woman carries a genetic change on the X chromosome, which is passed onto a child (X-linked conditions). Some examples of single gene conditions include Cystic Fibrosis, Fragile X syndrome, Spinal muscular atrophy, Thalassaemia and Sickle Cell Disease. Armed with this information, patients can make informed decisions about their reproductive options.

Why have the test?

Most children with single gene conditions are born into families with no known affected family members. Having the information in advance allows all reproductive options to be considered, including prenatal testing, pre-implantation genetic testing of embryos created in an IVF cycle, paediatric testing if symptoms arise, and other options such as egg or sperm donation, adoption or choosing not to have children.

What is the difference between “3 condition or 3 gene” and “expanded” carrier screening?

The “3 condition” or “3 gene” carrier screen, tests common conditions in the Australian population: Cystic Fibrosis (CF), Fragile X syndrome, and Spinal Muscular Atrophy (SMA). About 1 in 200 reproductive couples find out they have a high chance of passing on one of these conditions to their child.

There is no out-of-pocket cost for Medicare eligible individuals. The testing is sequential: only female partners are eligible for the test in the first instance, with males becoming eligible once their female partner has been identified as a carrier of SMA or CF. Each set of results takes approximately 2-4 weeks from sample receipt in the lab, which means that the test results overall may take 4-8 weeks to identify a reproductive couple with a high chance of having an affected child.

At Repromed we also provide and strongly recommend an expanded carrier screening panel which tests for hundreds of genetic conditions. The list of genes tested includes the 3 listed above as well as hundreds of others that are equally as serious - from Thalassemia to Duchenne Muscular Dystrophy (DMD). Although individually rare, these conditions are collectively common and the proportion of reproductive couples with a high chance result is increased to 1 in 50: around 5 times the detection rate of 3 gene carrier screening alone. The result takes approximately 4-6 weeks from sample receipt in the lab and tests both partners at once when performed as a couple test.

Blood or Swab?

DNA samples can be collected through a blood test or a saliva swab. Blood samples can be collected at Repromed. We also provide a “no needles, no fuss” option, where patients can follow a QR code on the Carrier Screening Fact Sheet, Genetics Request Form or visit our website to purchase a saliva kit to be sent to their home.

What happens if a patient is a carrier or high risk?

If a patient is identified as a carrier of SMA or CF, they will be contacted by our genetic counselling team to initiate bulk billed partner testing. If a patient is identified as a Fragile X premutation carrier, our genetic counselling team will be in touch to discuss their testing and reproductive options.

If any of our expanded test results indicate a couple are at increased chance of having a child with a single gene condition, our experienced genetic counselling team will make contact to discuss all of their options, such as IVF with pre-implantation genetic testing or further diagnostic testing for already pregnant patients.

Whichever option patients chooses, the support from our genetic counselling team and the integration with our clinical services will mean that their experience is as smooth as possible. We are also able to connect patients with local public genetics services as required, through our extensive network of contacts in the genetics community.

Case Study

A 30 year old woman mentions she is planning pregnancy when seeing her GP for a routine cervical screening test. After discussing the merits of 3 gene vs. expanded carrier screening, she decides to go ahead with 3 condition screening. Her result is low risk for Cystic Fibrosis and Spinal Muscular Atrophy. Her Fragile X screen shows 75 CGG repeats, indicating she is a premutation carrier. She later recalls that her mother had a history of early menopause at age 35, although there is nobody in the family that has had Fragile X syndrome.

After discussing the implications for her own health and the chance of having a child with Fragile X syndrome, she decides to undertake a fertility assessment which shows that her AMH level is 3, indicating a potential low response to IVF treatment and an increased chance of premature ovarian insufficiency. She decides to conceive naturally and undertake prenatal testing in a future pregnancy, with testing in her first pregnancy showing a normal result for Fragile X.

Dr Tristan Hardy
Medical Director Genetics,
Monash IVF Group

Your Guide to PGT: The Game-Changer in Fertility

What forms of genetic testing are available in fertility treatment?

PGT-A, PGT-SR, PGT-M – it's like alphabet soup for embryos!

PGT-A screens for chromosome changes which may affect any embryos. PGT-SR is used for patients who have a structural rearrangement (translocation) of their chromosomes. And PGT-M is used for patients with a known single gene condition.

Why do we test embryos using PGT-A?

The fact is, embryos may look the same under the microscope – even if they do not have a typical number of chromosomes.

PGT-A screens for chromosome changes which occur at conception, usually due to an extra or a missing chromosome being present in an egg or sperm. As chromosome changes are a major cause of pregnancy loss either at the time of implantation or during pregnancy, PGT-A can help reduce the time taken to achieve a live birth. It can also help avoid the emotional and financial burdens associated with failed IVF attempts or pregnancy loss. Therefore, it may be considered for patients suffering recurrent miscarriage, over 35 years of age, or for those with repeated unsuccessful IVF cycles.

Why do we test embryos using PGT-SR?

Around 1 in 500 people in the general population, and perhaps 1 in 200 people in the population utilising IVF, have a structural chromosomal abnormality such as Robertsonian and reciprocal translocations, or chromosome inversions. They may not be aware of these abnormalities as they have not impacted their life in any way - until they try for a pregnancy.

Structural abnormalities in chromosomes can cause implantation failure or miscarriage. We recommend patients with fertility issues obtain a karyotype: although many will have a clinical indication such as recurrent miscarriage, low sperm count or diminished ovarian reserve, but equally many will not present with any issues other than delay in achieving pregnancy.

PGT-SR is performed on couples with known structural rearrangements to help identify embryos that have inherited unbalanced versions that may lead to lack of implantation, miscarriage or a genetic condition. PGT-A can also be performed on PGT-SR samples to identify common chromosome changes which impact the chance of implantation and miscarriage.

Why do we test embryos using PGT-M?

At Repromed, we offer advanced genetic testing of embryos to patients who are carriers of a genetic condition or are affected by a genetic condition.

This may be when both partners are known carriers of a recessive condition such as those tested for by Carrier Screening, when one partner is affected with a dominant condition, or when the female partner is a carrier of an X-linked condition.

Any genetic condition where a genetic test can be performed on an adult can be tested in an embryo, but the type of genetic test will be different and involve an additional test design process before the couple can proceed to IVF with PGT-M. Our genetic counselling team will assist patients in considering all reproductive options, including preimplantation genetic testing.

PGT-M can be used to screen for most known inherited genetic conditions including (but not limited to):

- Cystic Fibrosis
- Fragile X
- Spinal Muscular Atrophy
- Alpha or Beta-thalassaemia
- Duchenne Muscular Dystrophy
- Huntington's disease
- Hereditary breast/ovarian cancer (BRCA1/BRCA2)

PGT-A is also performed concurrently on PGT-M samples to identify common chromosome changes which impact the chance of implantation and miscarriage.

"Most genetic conditions where a genetic test can be performed on an adult can be tested for in an embryo."

Behind the Scenes

Ever wondered how we do the "magic"? Dr Emily Button - Head Clinical Scientist (Genetics), helped to shed some light on this topic.

"First, we need DNA from each reproductive partner – either a blood test, or a "no needles, no fuss" option with a saliva swab. When embryos have been grown to Day 5 or 6, cells are removed from the outside layer of the embryo (via an embryo biopsy) then they are off to the Repromed Genetics Lab. The embryos are frozen while this testing is taking place.

The DNA from the embryo biopsy is amplified to millions of copies from just a handful of cells. Then we make a roadmap of genetic markers in the embryo and compare these to the parental blueprint.

For all patients, we can determine if there may be an extra or missing chromosome (PGT-A). For PGT-SR patients, we can also identify inherited structural rearrangements. For PGT-M, we can recognise which embryos have inherited the genetic variant known in the family.

It takes 3-4 weeks to receive the results from this testing, after which a fertility specialist can discuss with the patient which embryos are most suitable to transfer.

At Repromed, we are proud to have an in-house on-site Genetics Department that supports patients. If you have any questions for wish to learn more, please feel free to reach out to us at Repromed."

Case Study

A 36 year old female has a family history of breast and ovarian cancer, with his mother dying in her early 40s from ovarian cancer and sister recently being diagnosed with breast cancer at 32. She has a positive result from genetic testing showing a BRCA1 variant. When planning pregnancy with his wife (above), the husband seeks an opinion from the local Cancer Genetics clinic to have cascade testing which shows he also has the BRCA1 variant.

After discussing the implications for his own health and the reproductive options available, he attends the IVF unit with his partner to arrange IVF with PGT. In the process of test design, they are offered expanded carrier screening which identifies that his wife is a carrier of Duchenne Muscular Dystrophy. They successfully design a test for both conditions in embryos, selecting embryos for transfer that are low risk for BRCA1 and not predicted to be affected by Duchenne Muscular Dystrophy. They conceive on their third embryo transfer and go on to confirm the PGT result with prenatal diagnosis during pregnancy.

Dr Tristan Hardy
Medical Director Genetics,
Monash IVF Group

Your Guide to NIPT: Empowering Expectant Parents

Prenatal cell-free DNA screening, previously known as Non-invasive Prenatal Testing (NIPT) or Non-invasive Prenatal Screening (NIPS) is a simple blood test for pregnant patients, available from 10 weeks gestation. Repromed's prenatal cell-free DNA test is called 'Nest' and screens for common and rare chromosomal conditions, giving parents-to-be more information about the chance of having a child with a chromosome condition.

What does it test for?

The Nest test can provide accurate information about the most common chromosome changes seen in pregnancy - Trisomy 21 (Down syndrome), Trisomy 18 (Edwards syndrome) and Trisomy 13 (Patau syndrome).

If a patient receives a high-risk result, our team of experienced prenatal genetic counsellors are available to guide patients through the next steps at no cost.

Our genome-wide Nest+ option checks for significant changes across all chromosomes with no additional charge. Changes in uncommon chromosomes can rarely affect the pregnancy, but more commonly affect placental health, leading to issues such as intrauterine growth restriction.

We perform this test throughout Australia for our patients through our specialist women's ultrasound clinics, who can provide the test alongside a viability ultrasound and first trimester biomarker screening for assessment of pre-eclampsia risk. Providing a comprehensive first trimester assessment.

Why have the test?

NIPT is recommended as an available screening option for all pregnant individuals regardless of age. Typically, it should be performed as a standalone test, but can be performed following a high-risk conventional screening result.

Compared with some traditional prenatal screening methods, Nest is highly accurate in detecting chromosomal abnormalities, with a low false-positive rate. Unlike other invasive prenatal testing methods like amniocentesis or chorionic villus sampling (CVS), Nest is a simple blood test for the pregnant person without risk to the fetus.

Ultimately, a Nest test can help expectant parents make informed decisions about their pregnancy, allowing them to better prepare for the arrival of their child.

How is it performed?

We test the fragments of genetic material from parent and baby in a blood sample, looking for any extra or missing information on chromosome pairs.

"NIPT is a simple blood test for the pregnant person without risk to the fetus."

Should a patient perform Nest after having PGT?

Even if PGT-A has been performed and embryos with the typical number of chromosomes have been selected for transfer, there is still a small risk of chromosomal abnormalities occurring during early fetal development. Nest provides an opportunity to screen for these abnormalities during pregnancy, allowing for early detection and appropriate management, such as further diagnostic testing. Nest can also offer additional reassurance and peace of mind.

Case Study

A 38 year old woman has had a previous pregnancy with Trisomy 21 and requests cell-free DNA screening using genome-wide Nest+. This shows a low risk for Trisomy 21, 18 and 13 but a high risk for Trisomy 16. After receiving counselling on the likelihood of an ongoing affected pregnancy and the importance of amniocentesis to check the fetal cells rather than placenta in the setting of an uncommon chromosome condition, she books in for an amniocentesis at 15 weeks. This shows a normal karyotype for the baby (46,XY) and the obstetrician informs her that the trisomy 16 cells are most likely confined to the placenta, which is the source of cell-free DNA during pregnancy.

Because Trisomy 16 is associated with adverse pregnancy outcomes such as intrauterine growth restriction and stillbirth, she has additional monitoring with obstetric growth scans planned at 28 weeks onwards. These demonstrate that the baby is <3rd centile and she has increasing frequency of fetal monitoring and a planned early delivery at 36 weeks.

Book your place at our 2024 Reproductive Health Summit in Adelaide

When

Saturday 26 October, 2024
8:00AM for an 8:30AM start - 3:00PM

Where

Adelaide Entertainment Centre,
98 Port Road, Hindmarsh

RSVP

Please register by scanning the QR code or visiting **repromed.com.au/gp-seminars**

We're excited to be once again host our Reproductive Health Summit in Adelaide.

Please join us for what will be an informative yet relaxed session where we will cover the gamut of fertility investigations and causes of sub-fertility impacting today's patients.

The Summit will also include an open Q&A session with Dr Koch.

Hosted by
Dr Juliette Koch
Medical Director – Repromed

Topics to be discussed include:

- Supporting the emotional well-being of fertility patients
- How egg freezing empowers women: a practical guide for General Practitioners
- Breaking barriers: understanding male infertility
- How to manage Doctor Google
- Navigating donor program fertility options
- Unlocking Genetics: A primer on Genetic Carrier Screening for General Practitioners
- Identifying Endometriosis and Adenomyosis via Ultrasound
- Open Q&A

EDUCATIONAL ACTIVITIES
5.5
hours

RANZCOG CPD APPROVED ACTIVITY
MAY 2024 · MAY 2025

ACRRM CPD ACCREDITED ACTIVITY
2023-2025

RACGP
(Self Reported Activity)

Clinical Resource Form

Repromed is committed to sharing our expertise and providing you with support materials for your clinical practice.

- [ ] **Fertility and Reproductive Genetics Update**
  - [ ] at your clinic
  - [ ] webinar
- [ ] **Repromed Clinical Tools**
  - [ ] Fertility investigation wheel
- [ ] **nest (Non-invasive Prenatel Test) Information Pack**
- [ ] **Genetic Carrier Screening Information Pack**
- [ ] **Repromed Pens and Notepads**

Clinical Fact Sheets:

- [ ] Our clinical team, success rates and services
- [ ] Elective egg freezing
- [ ] Endometriosis and infertility
- [ ] Semen analysis / male infertility
- [ ] AMH
- [ ] PCOS and infertility

Pathology Request Forms:

- [ ] AMH
- [ ] Semen analysis
- [ ] nest

Patient Information Brochures:

- [ ] Elective egg freezing
- [ ] Fertility health check
- [ ] nest parent to be brochure
- [ ] Preparing for pregnancy
- [ ] Genetic at-home carrier screening
- [ ] Free nurse chat

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