# THE FACTS ON FERTILITY.

SUMMER 2019

## COMPASSION AND CUTTING EDGE SCIENCE AREAS THE KEYS TO FERTILITY TREATMENT SUCCESS.

**by Professor Kelton Tremellen, Medical Director**
**MB BS(Hons) PhD FRANZCOG CREI**

The success of fertility treatment, like all areas of medicine, is the net result of a team effort. The doctor's clinical and technical skills, the nurse's ability to guide patients through what must initially appear as a daunting number of steps in treatment and the embryologists nurturing of the patients precious gametes and embryos. These scientists, the unsung heroes of IVF, are so critical to a successful IVF program and therefore a key factor to consider when deciding which clinic to send your patients to. Here at Repromed we have eight PhD scientists specialising in diverse areas ranging from embryology, genetic analysis of embryos, andrology and endocrinology. As a result Repromed Darwin provides the most comprehensive scientific range of Assisted Reproductive Treatment (ART) services available, with all endocrine, embryo genetic analysis and andrology services being performed 'in house'. This ensures that Repromed Darwin can provide rapid turn around of results and have total control over service quality. No other clinic in South Australia or the Northern Territory comes close to this in terms of the depth of scientific PhD experience and breadth of treatment options.

Research is given a high priority at Repromed as we believe that it not only benefits patients' clinical care, but also enriches the work experience of our staff. Research at Repromed has been integral in the development of many clinical advances that have benefited patients around the world. In our next newsletter we will touch on one of those advances- non invasive pre-implantation genetic screening. More recently, Professor Tremellen's publication on sperm oxidative stress was recognised as a citation classic, ranked as the 9th most quoted paper in the field of andrology in the last hundred years (1). This accolade, and his invention of the male antioxidant therapy Menevit, is just one example of where Repromed staff are making a meaningful difference in reproductive medicine through their applied clinical research.

Finally, Dr Deirdre Zander-Fox (Scientific Director Dulwich) and Professor Tremellen were recently awarded the runner up prize for best paper published in 2017 in the journal Reproductive Biomedicine Online (2). This journal was initiated by the Nobel Prize winning scientific pioneer of IVF- Professor Robert Edwards. It was therefore appropriate that the prize was presented to Professor Tremellen at a conference in London celebrating the 40th anniversary of the birth of Louise Brown, the world's first IVF baby.

This prize winning research article explored the underlying mechanisms behind why miscarriage is increased in obese women - specifically does the problem lie with the embryo or the uterine environment. In order to examine this question Repromed analysed the outcomes of 125 biochemically confirmed pregnancies in which a high quality euploid (genetically normal) embryo was transferred. The primary findings were two-fold. Firstly, irrespective of the underlying cause of infertility, the rate of miscarriage of good quality embryos increased with BMI - confirming the presence of an underlying uterine pathology. Secondly, uterine endometriosis (adenomyosis) was more commonly seen in overweight and obese women compared to their lean counterparts, with adenomyosis being recognised as a risk factor for miscarriage. Fortunately, more recent work by Repromed and Flinders University has shown that hormonal pre-treatment (ultra-long down regulation) of adenomyosis can significantly reduce the risk of miscarriage (3).

In 2019 Repromed has continued to strive to offer high quality clinical care for your patients, drawing on our leading clinical and scientific expertise, world class facilities and cutting edge research. On behalf of Repromed I would like to thank all our referrers and wish them and their patients a happy and successful year.


**KELTON TREMELLEN.**

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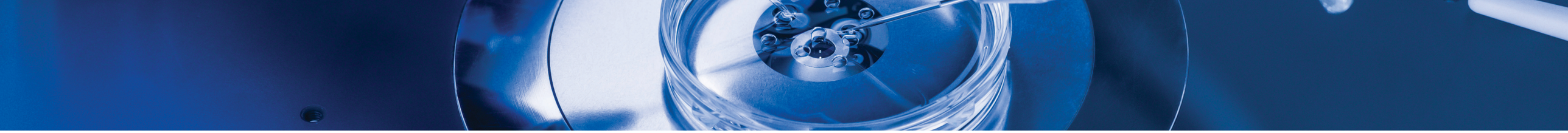
Reproductive Endocrinology
And Infertility Sub-specialist MBBS(Hons), PhD FRANZCOG, CREI, Grad Cert Mgmt



**References** 1. Bullock N, Ellul T, Bennett A, Steggall M, Brown G. The 100 most influential manuscripts in andrology: a bibliometric analysis. Basic Clin Androl. 2018 12;28:15. 2. Tremellen K, Pearce K, Zander-Fox D. Increased miscarriage of euploid pregnancies in obese women undergoing cryopreserved embryo transfer. Reprod Biomed Online. 2017;34(1):90-97. 3. Stanekova V, Woodman RJ, Tremellen K. The rate of euploid miscarriage is increased in the setting of adenomyosis. Hum Reprod Open. 2018; 1:1-8



# ONCO-FERTILITY.

**by Dr Vamsee Thalluri.**

In Australia, approximately 2% of women of reproductive age are diagnosed with cancer, with 50% of these women requiring gonadotoxic treatment.

With earlier detection of cancer, as well as advancements in treatment, we are seeing significant improvements in survival rates and thus it is important we not only focus on treating the disease but also on ensuring optimal quality of life afterwards. For many women this includes the ability to start or grow their family. Unfortunately one of the potential side effects of cancer treatment is premature ovarian failure.

Treatment effects on future fertility depend on the mode of cancer treatment, the drugs used and the dose and duration of the agents used. Typically the main treatments that are associated with significant detrimental effects on fertility are the alkylating chemotherapy agents (eg Cyclophosphamide) as well as abdominal/ pelvic radiation therapy.

Following a diagnosis of cancer where the patient is expected to undergo gonadotoxic treatment, counselling regarding the potential effects on future fertility should be offered. The opportunity to proceed with fertility preservation treatment can then be discussed and the patient can decide whether it is something they wish to do.

For women the option for fertility preservation will typically mean controlled ovarian stimulation in order to freeze oocytes or embryos. Approximately 12-14 days is required to complete this process and whilst a typical IVF cycle normally starts with the patient's menses, in an emergency fertility preservation cycle where time may be of the essence, we are able to commence the stimulation immediately as part of a 'random-start protocol'.

In breast cancer there is typically a 6 week break between surgery and commencement of adjuvant chemotherapy, this is often a good time to complete a fertility preservation IVF cycle should the patient wish to do so. Research has shown that undergoing an IVF cycle for fertility preservation does not cause the cancer to progress or impede the ability to proceed straight into cancer treatment. Certainly, the decision to proceed with fertility preservation treatment is made as part of a multi-disciplinary team and in close conjunction with the treating Surgeon and/or Oncologist.

During the counselling process it must be made clear that fertility preservation treatment is not a guarantee of future children. 20-40% of women with breast cancer treated with chemotherapy will undergo early menopause and unless these women had oocytes or embryos frozen prior, they will have little choice but to consider egg donation or adoption should they wish to have children in the future.

Other options for fertility preservation include giving the patient a GnRH agonist during their chemotherapy treatment. This is thought to put the ovaries into a quiescent state and thus potentially reduce the impact on the ovarian reserve. Whilst such treatment has become rather popular in recent times the research data showing benefit remains limited and thus it is still considered to be controversial. Further prospective trials and ideally randomised controlled trials are needed to determine if GnRH agonists are an effective pharmacological treatment for the purposes of fertility preservation.

For men diagnosed with cancer, we would advise freezing sperm prior to undertaking gonadotoxic cancer treatment.

**At Repromed we are dedicated to providing an Onco-Fertility service that allows urgent clinical appointments and provision of fertility preservation treatment at no out of pocket expense to the patient, with the exception of day surgery and anaesthetic fees if applicable, via outsourced providers. Patients with private health insurance may be covered for all or part of the day surgery & anaesthetic fees.**

## VAMSEE THALLURI.

Fertility Specialist / Gynaecologist

MBBS, MRANZCOG, CREI Fellow

Dr Thalluri completed his schooling in Adelaide and went on to study Medicine at The University of Adelaide. Having completed RANZCOG Specialist Training Program, he is now undertaking further experience to obtain the highest qualification available in Australia in the field of reproductive medicine and infertility (Certificate of Reproductive Endocrinology and Infertility – CREI).

Dr Thalluri has published in peer reviewed journals and also presented at the Fertility Society of Australia's national conference.

# SIGNIFICANT IMPROVEMENT TO REPORTING CAPABILITIES FOR NEST.

**by Dr Leanne Pacella-Ince**
**BHSc (Hons), PhD, Scientific Director**

In November 2016 Repromed launched nest: our in-house non-invasive prenatal screening solution.

Since this time nest laboratories are proud to have provided reassurance and important genetic information to over 30,000 expectant Australian mothers.

In addition to screening for trisomy 13 ,18 ,21 and sex chromosomes, nest is now able to screen all 22 autosomes and the sex chromosomes and identify significant duplications/deletions (down to 7Mb).

This new all-chromosome screening option called **nest+** is available at no additional cost and provides the same fast turnaround and reliability as the standard nest test.

**nest+** allows screening for rare autosomal trisomes that may occur in a small proportion of pregnancies (<0.5%). These rare chromosomal abnormalities may lead to varying degrees of fetal abnormalities requiring prenatal diagnosis, or provide important information regarding placental health and the risk of pregnancy complications such as stillbirth, IUGR and pre-eclampsia.

With the introduction of **nest+** you now have the opportunity to offer your patients a more comprehensive screening option. nest laboratories will also continue to offer your patients the standard nest 13, 18, 21 screening only as an option.

### NEST SINGLETON + TWIN PREGNANCIES

- Aneuploidy screening of chromosomes 13,18,21
- Sex chromosome aneuploidy screening (singleton only)
- Fetal gender reporting (on request)

### NEST + SINGLETON PREGNANCIES ONLY

- Aneuploidy screening of all 22 autosomes
- Sex chromosome aneuploidy screening
- Fetal gender reporting (on request)
- Duplication /Deletions >7Mb)

**nest and nest+ are screening tests only and for patients with a high risk result, subsequent clinical management should include genetic counselling and invasive diagnostic testing.**

To order your new starter pack with updated patient brochures, clinician information and request forms please contact the nest laboratories on 8333 8172 or email enquiries@nestscreen.com.au

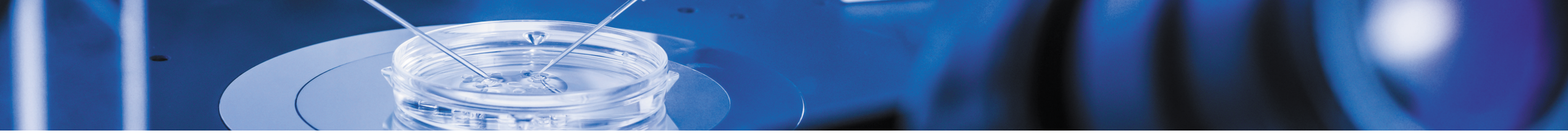
## DR LEANNE PACELLA-INCE.

Leanne joined Repromed in 2007 and is Scientific Director of Repromed Darwin, Fertility Tasmania and Deputy Scientific Director of Repromed South Australia.

A fully qualified Embryologist, prior to becoming the Scientific Director of Darwin Leanne was the Genetics Co-ordinator for Repromed.

Completing her PhD in 2014 through the University of Adelaide's School of Paediatrics and Reproductive Health for which she was awarded the Dean's Commendation for Thesis excellence. Her PhD focused on the contribution of perturbed granulosa and cumulus cell metabolism and mitochondrial protein levels to the poor IVF outcomes seen in women undergoing IVF with either reduced ovarian reserve or advanced maternal age.

In 2016, Leanne was awarded the Scientist in Reproductive Technology Established Scientist Award. With published papers in peer reviewed journals, Leanne is also an honors supervisor through the Adelaide University's Department of Obstetrics and Gynecology as well as an Australian Institute of Medical Scientists Assessor for IVF Embryologists.



# RECENT CHANGES TO THE GUIDELINES FOR ASSESSMENT AND MANAGEMENT OF POLYCYSTIC OVARY SYNDROME (PCOS) HAS AGAIN BROUGHT THIS CONDITION TO THE FOREFRONT.

**Dr Juliette Koch helps to explain PCOS and how it can affect female fertility.**

### Q: What causes PCOS?

**A:** PCOS stands for Polycystic Ovary (or Ovarian) Syndrome and it is a hormonal disorder that affects up to 1 in 5 women world wide. Often a complex condition to identify, PCOS has several contributing symptoms however a patient does not have to have all of the symptoms to be diagnosed with PCOS. In fact, very few women have the same set of symptoms.

To date the causes of PCOS are still unknown. No single gene has been found to cause PCOS, so the link is likely to be complex and involve multiple genes however there are indicators that suggest family history, insulin resistance, lifestyle and/or environment do play a part.

### Q: Is PCOS more prevalent in certain age groups?

**A:** Interestingly 12-18% of females of reproductive age are thought to have PCOS – therefore being able to identify them early and manage their condition will give them greater options about if and when to start a family.

### Q: How does common is PCOS in families?

**A:** Immediate relatives (sisters or daughters for example) of females with PCOS are 50% more likely to have PCOS themselves.

### Q: How does PCOS affect a female's fertility?

**A:** Women with PCOS often have high levels of androgens and insulin which can affect their menstrual cycle and prevent or disrupt ovulation and thus making it more difficult to conceive naturally. And some women with PCOS can have a greater risk of miscarriage.

### Q: What are the symptoms of PCOS?

**A:** PCOS can be a complex condition to identify because there are several indicators and a patient does not have to present with all of them to be diagnosed with the condition.

Symptoms can include irregular or missing periods, growth of excessive facial or body hair, scalp hair loss, acne and/or oily skin, and sudden or unexplained continuous weight gain.

### Q: The guidelines for PCOS Assessment recently changed – is that correct?

**A:** Yes, the international guidelines were released at the ESHRE meeting in Rome in July 2018. The guidelines were produced in collaboration with over 1600 health professionals and 1500 women and coordinated by the NHMRC and the Australian Centre for Research Excellence in PCOS in collaboration with the American Society of Reproductive Medicine and the European Society of Human Reproduction.

The aim of the guideline is to promote accurate diagnosis, optimal consistent care, prevention of complications and an improved patient experience and health outcomes for women with PCOS.

### Q: What are the important updates addressed in the guidelines?

**A:** The importance placed on irregular cycles and hyper-androgenism. Free androgen index is suggested as the most reliable biochemical marker and doctors are encouraged to exclude other causes if the FAI is much higher than the reference range.

Whilst the guideline endorses the Rotterdam criteria in adult women, the ultrasound criteria for polycystic ovaries on ultrasound, has been modified. Polycystic ovarian morphology (PCOM) on ultrasound has been addressed and the criteria for diagnosis has increased from 12 follicles to 18 per ovary or a volume of 10mls or greater. Standardised measurement and reporting of pelvic ultrasound has been recommended. AMH has not been endorsed as a diagnostic tool. With improved standardisation of assays and large scale validation in different populations and ethnicities, AMH may be a useful tool in the future.

The diagnosis of PCOS in adolescence is hampered by the frequency of irregular periods, acne and PCOM in this population. Consumer groups have emphasised the profound psychological impact of the diagnosis and the guideline emphasises the need for caution in this group. The recommendation is only to make the diagnosis at greater than 2 years post menarche and to place importance on hyperandrogenism as a key component. The recommendation in this age group is not to perform ultrasound but to do a baseline hormone profile before starting the ocp and recommending further assessment in years to come.

Assessment of complications of PCOS is important and the recommendation is baseline lipids, yearly weight, BP and 1-3 yearly glucose tolerance test based on other risk factors. All women planning pregnancy with PCOS are recommended to do an oral glucose tolerance test. Health professionals also need to consider and screen for other potential complications such as obstructive sleep apnoea and endometrial cancer, with referral to the appropriate specialist.

### Q: What do the guidelines recommend as front line treatment?

**A:** The oral contraceptive is recommended as first line treatment for both menstrual irregularity and hyper-androgenism but no particular preparation is considered superior. Women are encouraged to use the lowest effective dose and be cautious of venous thromboembolism (VTE) with higher dose preparations or risk factors for VTE.

Metformin can be used for women with BMI →25 and women in ethnic groups which are at high risk of impaired glucose tolerance. Some good quality studies demonstrate improvement in lipids, testosterone, glucose and insulin levels with metformin.

With regards to fertility and ovulation induction, this guideline recommends the use of letrozole as a first line agent due to a superior live birth rate (40-60% higher) and lower multiple pregnancy rate than clomiphene. Second line treatment involves the use of FSH injections or laparoscopic ovarian drilling. IVF is effective for women with PCOS and multiple pregnancy can be reduced with single embryo transfer. Women with PCSOS are at increased risk of ovarian hyperstimulation and this needs to be minimised. Bariatric surgery and anti-obesity agents remain experimental.

Healthcare should be provided in partnership with women and promote self- empowerment and education. Healthy lifestyle is important to prevent long term complications and achievable goals such as 5% reduction in body weight can yield clinically relevant improvements. The guideline emphasizes the need for healthcare interactions about healthy lifestyle, diet and exercise to be respectful, patient-centered and take into account women's personal, cultural and ethnic differences.

### Q: Do you have any final words on PCOS?

**A:** It important to understand the increased rate of depression, anxiety, eating disorders and body image problems that women with PCOS can suffer. Women with PCOS may require multidisciplinary care from their GP, specialists in endocrinology and infertility, and allied health clinicians such as psychologists, dieticians and exercise physiologists. Most importantly however, the promotion of self-care and use of peer support groups should be encouraged.


**JULIETTE KOCH.**

Senior Fertility Specialist / Gynaecologist

MBBS, FRANZCOG, CREI, MRepM


Born and raised in Adelaide, Dr Koch was lured by the bright lights of Sydney as a young doctor, where she was quick to find her passion for women's health whilst working at the Royal Hospital for Women.

After an obstetrics stint in Outback Australia, Dr Koch committed to specialising in Obstetrics and Gynaecology, and she has not looked back; opting to go beyond her six-year specialist training to complete a rigorous Masters in Reproductive Medicine and three-year subspecialist qualification in Reproductive Health to ensure she remains at the very forefront of her field when it comes to helping people have, or extend their family.

Most recently, Dr Koch has worked as the Deputy Director of the Department of Reproductive Medicine at the Royal Hospital for Women in Sydney, providing services in fertility, menopause and gynaecology.

Dr Koch was also a lecturer at UNSW and training supervisor for subspecialty training in infertility and endocrinology. Warm and approachable, Dr Koch is extremely thorough in her investigation and management of infertility and the emotional ups and downs along the way.

Having recently returned to Adelaide with her husband and three boys to be closer to family, and to enjoy the wonderful lifestyle that Adelaide offers. Highly qualified, but also committed to a personal, caring and thorough approach, she is a highly valued specialist within the Repromed team.



## ALICE SPRINGS.

Repromed is a proud local team providing local care. With a world-class lab located in Darwin, Repromed has been providing local care to Northern Territorians for over 25 years. Our highly qualified team of doctors, nurses and scientists are all proud Territorians, meaning your patients do not have to travel outside of the Territory for their fertility treatment.

Repromed is also pleased to provide fertility consulting bi-monthly in Alice Springs by Dr Nicky Purser. Appointments for Dr Purser can be made by calling 8495 4211.

### DR NICKY PURSER.

MBBS, FRACGP, DRANZCOG

After graduating from the University of Queensland in 1986, Dr Nicky Purser worked in country Queensland before moving to Darwin in 1990 to work at Royal Darwin Hospital. Since then, she has lived and worked in most NT towns – Darwin, Katherine and Gove as well as four years in Alice Springs.

Since 2000, Dr Purser has been working in General Practice in Darwin, with special interests in Women's Health, Paediatrics and GP Anaesthetics. She has been very pleased to be able to expand her interest in Women's Health with her commencement at Repromed in May 2009.

### DR Stephanie Girle.

MBBS, DRANZCOG, FRACGP

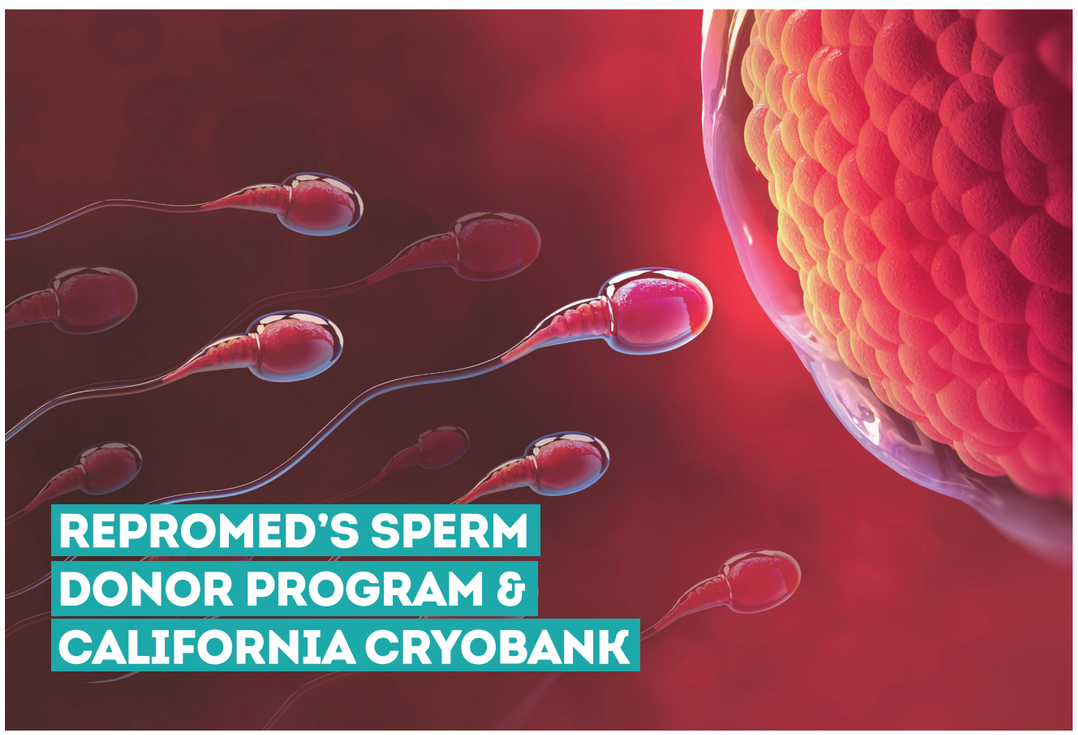
Dr Stephanie Girle completed her medical degree in Queensland. Moving from Cairns to Darwin in 1982 she worked as a flying doctor where she met her pilot husband. Dr Girle then spent 10 years in the Obstetrics and Gynaecology Department of the Royal Darwin Hospital developing her interest in women's health.

Dr Girle has consulted at the Darwin Repromed clinic since 1993. Stephanie left her successful general practice in Fannie Bay in 2009 to concentrate solely on her passion for infertility services in the Northern Territory.

### Infertility

**The inability to conceive after a year of unprotected intercourse, is a common concern for both men and women as approximately 1 in 6 couples will experience difficulties when trying to conceive.**

**For the vast majority of couples, they will fall pregnant naturally within the first 12 months of trying however research tells us that of the couples struggling to fall pregnant, 40% will be due to problems with sperm function, so called male factor infertility.**



## REPROMED'S SPERM DONOR PROGRAM & CALIFORNIA CRYOBANK

Recent changes to legislation has meant a person can not be refused fertility treatment based on their sexual orientation, gender identity, marital status or religious beliefs.

Women also no longer need a medical diagnosis of infertility to be considered for fertility treatment. This has given single females wishing to solo parent and same sex female couples the opportunity to become parents with the use of donor sperm.

In the Northern Territory, Repromed has exclusive access to California Cyrobank, who has over 40 years of reproductive experience, for high quality, ID disclosure sperm donors who comply with Australian guidelines.

Repromed has a dedicated Donor Team who work with both recruited donors and recipients. Our counsellors provide in-house ANZICA certified counselling, as well as our on-site doctors, nurses and laboratory services – ensures Repromed is fully equip to treat women with our donor program up to the average age of natural menopause which is taken to be 52 yrs.

### QUICK FACTS:

- A child born as a result of donation is considered to be a child of the Recipient/s. The Donor has no legal parenting rights or responsibility (including financial) for the child.
- Both parents (if in a relationship), or just the mother (if solo parenting) will be named on the birth certificate - donor's details are never listed.
- All Clinic Recruited Sperm Donors must be prepared to be contacted annually by Repromed to ensure their contact and medical details are up to date.
- All donors must be able to be identified to a donor conceived child from the age of 18 (at the child request).



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