

TREATMENT
CYCLE
HANDBOOK

PIVET MEDICAL CENTRE

ASSISTED REPRODUCTIVE
TECHNOLOGY PROGRAM

Welcome to
PIVET Medical
Centre

Introduction

At PIVET Medical Centre we strive to provide the highest level of care with the infertility treatment programs we offer.

This booklet has been designed to assist you by providing information about the various procedures available in the infertility program.

Hopefully it will be useful in answering some of the questions that may arise during your treatment.

Please liaise with clinical, nursing and counselling staff should you have any further questions in relation to your procedures.

We are here to help you.



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INITIAL INVESTIGATIONS & PREPARATION FOR TREATMENT

1. INITIAL APPOINTMENT

Both partners (where applicable) will be required to attend for the initial consultation. We require a referral from your doctor stating both partners names (where applicable). GP referrals last for 12 months whilst a specialist referral is valid for only 3 months.



At your first appointment with a PIVET Clinician (doctor), your medical history will be discussed along with any previous fertility treatment you may have undertaken. A copy of any information regarding previous fertility treatment may be helpful for your PIVET medical record, including operation reports, ultrasounds and previous blood test results.

A physical examination (on both partners, where applicable) will be performed. Female partners will undergo a cervical smear test and tests for vaginal bacteria and Chlamydia. If you have recently had a cervical smear test with your General Practitioner, a copy of the result must be provided. Investigations following will include an ultrasound scan for both female and male, blood and urine tests and for males, a semen analysis.

Please Note: Our PIVET Clinicians operates under a "team approach" and are rostered for set procedure lists in our day hospital, Perth Day Surgery Centre. Dependent on your allocated procedure day in our day hospital, you may be treated by a different Clinician from our team of Fertility Specialists. You can see your preferred Clinician for PIVET clinic consults - please request this from our friendly reception staff.

Blood / Urine Tests

Initial screening blood tests are carried out on both partners. Included in these tests are infectious disease screening such as HIV and Hepatitis, along with Chlamydia and Syphilis. Male and female hormone levels are also checked. Other tests include immunity to Rubella (German Measles), factors affecting blood clotting and determining autoimmune conditions (ANA, ACA and Anticoagulant screen) liver and thyroid function tests, full blood count / group, vitamin D, growth hormone factors, blood sugar levels, ovarian tumor marker (CA125), organic / inflammatory disease indicator (CRP), anti-sperm antibodies, ovarian reserve (AMH) and cytogenetics. Urine test screens for Ureaplasma, a bacteria found in the genital tract.

To obtain and discuss your results you will be required to see the doctor 2 - 3 weeks following your initial appointment. If you are planning to undergo an assessment cycle you can wait until you are booked in on Day 21 to see the doctor to discuss all the relevant results in one appointment. This will include obtaining results for blood tests, urine tests, ultrasound scans, semen analysis, assessment cycle and HyCoSy.

These investigations (excluding Cytogenetics and blood group) will be updated annually for both partners.



PLEASE NOTE

Blood tests and ultrasounds are carried out Monday to Friday, 7.30am to 9.30am, and waiting times could be up to 1.5 hours.

Ultrasound

This procedure looks at the female pelvic and abdominal anatomy. It is an internal trans-vaginal ultrasound than can identify anomalies such as fibroids and an unusual shaped uterus (womb). Male partners have an external ultrasound to identify the presence of any abnormal structures that may impact on sperm production and/or ejaculation. Your doctor will indicate the provider they wish you to attend. The majority of PIVET's new case ultrasounds are referred to Western Radiology.

Please arrange for this ultrasound to be performed at least **48 hours** before your next Doctors consult at PIVET Medical Centre to ensure your reports are available for your PIVET consultation. If you have any

questions or concerns regarding these ultrasounds please do not hesitate to contact PIVET to discuss this further.

SEMEN ANALYSIS

It is well documented that male factor infertility accounts for 30% of couples experiencing infertility. Therefore, the importance of a complete and thorough evaluation of the male partner cannot be underestimated, as ultimately clinical decisions are based on these results. Research has shown that laboratories do vary widely in their ability to provide accurate semen analyses. Semen analyses are best performed by scientists with extensive experience following the guidelines and criteria of the *World Health Organisation (WHO)**

The evaluation of the male partner begins with a simple laboratory test called a “semen analysis”, commonly known as a “sperm count.” However there is certainly more involved than just counting the sperm. Semen analysis is done on a sample of seminal fluid collected after masturbation. A semen analysis checks that sperm are present and helps identify if there is a problem with the number or quality of sperm being produced. The number, shape and movement of the sperm are measured under a microscope.

Generally, it is preferable that men produce their samples at PIVET Leederville, in our purpose built discreet private collection room, however it is possible to produce sample in the comfort of their own home and deliver the sample to the laboratory within 45mins. If you wish to use this option, please collect a specimen container from PIVET staff, along with the required paperwork and a specimen bag.

In order to obtain an accurate result, it is recommended that the analysis is performed after the couple has abstained from sexual activity for 2-7 days. Less than 2 days may result in a reduced sperm count. Abstinence periods of greater than 7 days results in a greater incidence of dead and morphologically abnormal sperm. It is a common misunderstanding of some male patients that they can improve their semen by “storing it up”.

In the laboratory, the PIVET scientists analyse the following parameters; *volume, pH, semen consistency, semen appearance, sperm concentration (how many sperm in each milliliter of semen), sperm motility (the number of moving and progression of sperm) and sperm morphology (the shape of the sperm head, mid-piece and tail)*. Other tests that can be done and might be requested by your doctor include, testing for the presence of antisperm antibodies in the semen and sperm DNA fragmentation.

Sometimes, more than one semen analysis is required since the testes are a very sensitive indicator of general health and as sperm are produced over a three month period, many factors can affect their production. Apart from when no sperm are seen (azoospermia), no single parameter of a semen analysis is indicative of fertility - it is an assessment of a combination of factors, including your background health that enable an overall prognosis to be made.

You will be given a semen collection questionnaire to fill out at the time of your appointment. The answers to these questions are needed for the reasons below:

- ★ **Time of collection?** Changes in sperm can occur over time, particularly after 1 hour.
- ★ **Days you have abstained from ejaculating?** Can affect the semen volume, sperm numbers and quality.
- ★ **Was the complete sample collected?** Can reduce semen volume and the numbers of sperm if some of the samples is spilt.
- ★ **Health in the past 3 months?** Maturation of sperm takes 3 months, so poor health during this time might be reflected in the sperm quality.
- ★ **Medications taken in the past 3 months?** A range of medications can affect sperm quality.
- ★ **Were lubricants or condoms used?** Lubricants and spermicides in condoms can affect sperm quality, so please do not use these.
- ★ **Have you been taking Menevit and for how long?** The use of Menevit may improve sperm quality.

- ★ **Did you spill any of the sample?** The largest quantity of sperm is found in the first part of the ejaculate. If you spill some of the sample, the semen volume will not be accurate and there is a possibility that the sperm count will not be accurate either.

The answers to these questions are very important and may provide information which may assist in the interpretations of your results.

NORMAL RANGES AND GLOSSARY OF TERMS USED

Measurements are made as part of the semen analysis need to be compared with reference values to allow decisions to be made regarding possible treatment strategies. The *World Health Organisation (WHO)* have published reference ranges which PIVET Laboratory measures your semen against. Normal ranges are outlined in the table below.

PARAMETER	NORMAL RANGE
Volume	> 1.5 ml
pH	≥ 7.2
Sperm Concentration	≥ 15 million sperm per ml
Normal Morphology (shape)	≥ 4%
Total Motility	> 40%
Progressive Motility	> 32%

- ★ **NORMOZOOSPERMIC** – is the term used when all semen parameters are within the normal range.

When parameters fall outside the normal ranges as defined above, the following terms are used:

- ★ **OLIGOZOOSPERMIA** – reduced number of sperm present.
- ★ **TERATOZOOSPERMIA** – reduced number of normal shaped sperm.
- ★ **ASTHENOZOOSPERMIA** – reduced number of motile / progressive sperm.
- ★ **AZOOSPERMIA** – no sperm present in entire ejaculate.

ANTISPERM ANTIBODIES

Some men develop antibodies to their own sperm, which may attack and weaken the sperm. Also, the antibodies may attach to the sperm and interfere with their movement or their ability to fertilise the egg. Your doctor may request that the laboratory test your semen for the presence of these antibodies.

DNA FRAGMENTATION - HALOSPERM

While the routine semen analysis can provide important information about male fertility such as sperm concentration and motility, it does not reveal any information about the integrity of the sperm's DNA. Sperm DNA can be damaged by exposure to chemicals, smoking, high temperature, and free radicals from normal

metabolism. Sperm DNA fragmentation has been associated with decreased fertilisation rate and miscarriages.

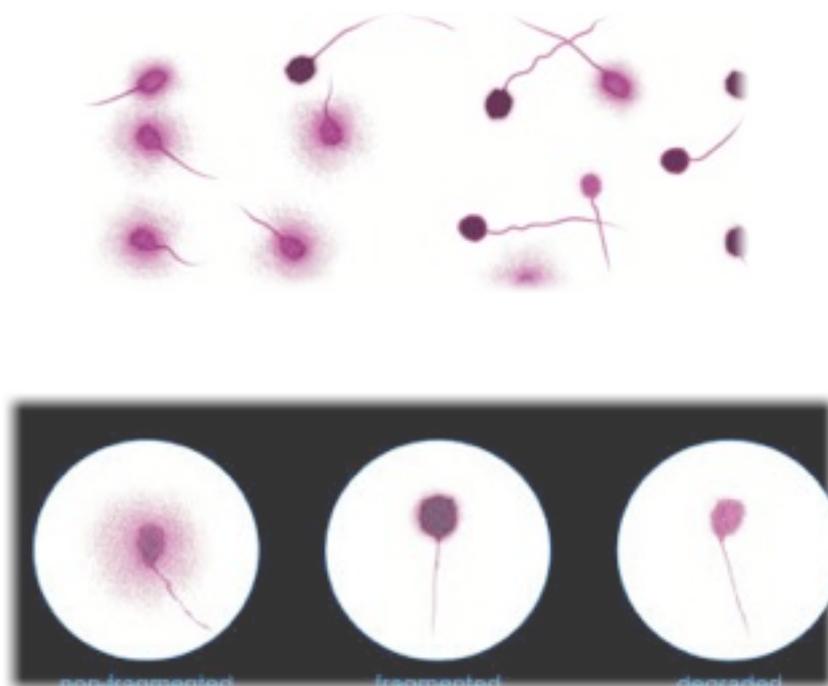
Research has shown that broken DNA in sperm does not disperse after acid denaturation. In contrast, normal sperm DNA disperses after special acid treatment to produce a halo of DNA chromatin around the sperm head.

The Halosperm test makes use of this property to differentiate sperm with normal DNA from those with fragmented DNA. Sperm are first exposed to a colored agent that stains the DNA within the sperm capsule. Subsequent acid treatment makes the sperm membrane leaky. Like a coiled spring upon release, sperm DNA disperses quickly through the leaky membrane to form a halo around the head of the sperm. If the DNA coil is broken, it does not leak readily through the sperm membrane and thus remains confined within the sperm head.

There have been a number of publications that link sperm DNA fragmentation to poor embryo development and pregnancy rates. This has been interpreted to mean that fragmented DNA in the sperm head are is less functional in the new embryo. Values of more than 30% fragmentation are considered undesirable. Please remember that tests such as the HaloSperm are relatively new and that the results are a guide only to semen quality and they need to be cautiously interpreted. It may be many years before the true implications of the test, if any, have been clearly determined.

If your HaloSperm test returns with a high value, you will need to discuss this with your fertility specialist. There have been some suggestions that HaloSperm values may be related to occupational and environmental factors while others have suggested repeated ejaculations may lower the value.

Your Fertility Specialist may request the test at any time but most likely it will be early in your management. Currently, you should expect this test to be requested at the same time as your first semen analysis. There will be a fee payable for this service (please refer to costing sheet). Poor results may mean repeated re-evaluation is required.



2. ASSESSMENT CYCLE & HyCoSy

Assessment Cycle

All fertility related patients attending PIVET will be required to undergo an Assessment Cycle. This is a tracking cycle that follows hormone levels in conjunction with follicle development for one month of the menstrual cycle.

It is an “information gathering” process and provides valuable assistance to the Fertility Specialist when it comes to determining treatment options. During the assessment cycle, you will undergo HyCosy procedure (see below) and Post Coital Test (PCT). These inclusions may be optional as determined by your Specialist.



To commence the Assessment Cycle you will be required to phone the clinic on Day 1 of your period to report that you are ready to start. The Assessment Cycle commences with a blood test on Day 2/3 of your menstrual cycle. Following this, around Day 5, you will require an ultrasound and a further blood test. You will then attend the clinic for blood tests and ultrasound every second or third day from Day 9 of your cycle until ovulation has been observed or the doctors feel enough information has been collected to provide you with treatment options.

After each test, the nurses will call / email and advise you of results and what is required next. Your HyCoSy will be performed before Day 12 in this cycle. The Theatre Coordinator will contact you to book the procedure.

Towards mid-cycle and when ovulation is predicted, a PCT test will be ordered. This test is performed when indicated by rising hormones and the presence of a dominant follicle. You will be instructed by the nurse to have sexual intercourse the evening before the test and then present to the clinic the next morning for a sample of cervical mucous to be collected. Whilst taking the sample, the nurse will be observing the cervix, the amount of mucous present and also the elasticity of the mucous. The sample will then be observed under the microscope to determine the presence of motile sperm.

The final phase of the test, requires “drying” the sample to observe the formation of ferning, which is indicative of increased oestrogen levels. A mid-luteal blood test around “Day 21” of your cycle concludes the assessment phase and this is when you will be required to attend for a *review consultation* and the results of the assessment cycle will be discussed with you and your partner (if applicable).

HyCoSy

A HyCoSy (Hystero Contrast Sonography) is an ultrasound investigation to check if the fallopian tubes are patent (open), ascertain the shape of the uterus and check for any abnormalities within the cavity of the womb. Ideally, it is performed immediately following your period. After the administration of an neurolept anaesthetic (also known as twilight sedation), a speculum is inserted into the vagina so that the cervix can be clearly seen. The cervix is cleaned before a fine tube is passed through the cervix into the uterus.

The speculum is then removed and a vaginal ultrasound is performed. Agitated saline is injected into the catheter and is seen (via ultrasound) passing into the uterus and through the tubes. If the fallopian tubes are blocked then this fluid will not be seen to pass through and out of the tubes. There may be some mild discomfort, which passes in hours, following the procedure.

This procedure is performed at PIVET in the day surgery unit, where you will be given an anaesthetic by a Consulting Anaesthetist. The Anaesthetist will take a health history and discuss the costs prior to the procedure. The procedure takes approximately 30 minutes, and approximately an hour recover from the anaesthetic.

The result of this test will be discussed with you in conjunction with all your other investigations at the time of your next follow-up visit with the doctor.



Risks and complications are very rare, but may include:

- Infection
- Moderate to severe discomfort
- Heavier than usual vaginal blood loss
- Anaesthetic complications

An alternate option of this test is a HSG (*HysteroSalpingoGram*) and this is booked via SKG Radiology. This option can be discussed with your PIVET doctor at your initial appointment.

3. DAY 21 APPOINTMENT

Just as all menstrual cycles commence on “Day 1”, all treatment cycles are set-up on “Day 21”. This is the ideal time to see the Fertility Specialist and make decisions regarding your assessment cycle, HyCoSy and initial investigations results.

An ultrasound will be organised for around day 21 of your cycle. You will be given a referral for this. This is to ensure there are no complications, usually from your previous ovulation, that may prevent you from commencing the planned treatment cycle.



IMPORTANT

Please note this appointment does not have to be exactly on Day 21, as this may fall over a weekend.

But if you use the terminology “I need to book a Day 21 appointment”, our reception staff will know to **organise** your ultrasound appointment **to be followed by** a clinic consult with your Fertility Specialist.

At this consultation your doctor will provide an overview of the treatment regimens that are recommended to assist with conception. These will be discussed along with any special features that may be offered to optimise the treatment cycle. These special features are used only when the need is identified (see ICSI / Assisted Hatching / Embryo Glue).

You are encouraged to take advantage of the doctor’s vast knowledge base and ask any questions you may have regarding your treatment cycle.

The treatment selected is designed to give you the best possible chance of conceiving and will be, in the first instance, the least complex and most effective for your condition. Please be sure that you have discussed your treatment program with your doctor and that you understand it fully before proceeding.

It is important to note that the female partner must have patent fallopian tubes for all treatment options with the exception of IVF & ICSI.

4. NATURAL CYCLE OVERVIEW

Menstruation

The first day of your cycle commences on the first day of your bleeding, known as menstruation, your period or 'Day 1'. Day one is determined when bleeding occurs before midday. If it first occurs in the afternoon, then the following day is deemed 'Day 1'. Menstruation is the shedding of the inner uterine lining or endometrium from the previous cycle.

Follicular phase

This commences from menstruation and involves the release of follicle stimulating hormone (FSH) and luteinising hormone (LH) from the pituitary gland in the brain. FSH is the hormone which stimulates the development of a follicle (fluid filled sac containing an egg).

Ovulation

The dramatic mid-cycle surge of LH causes the release of a mature egg from the follicle into the fallopian tube. During the next 12 - 24 hours the egg is fertile. The cervical mucus thins at this time to allow sperm to penetrate. It is during this time that the woman has the best chance of conceiving.

Fertilisation

The sperm travels through the cervical mucus, into the uterus and up through the fallopian tube to the egg. Despite millions of sperm being released only one sperm can fertilise an egg. Once an egg has been penetrated by a sperm, it becomes an embryo.

Implantation

If fertilisation occurs, the embryo travels towards the uterus where the embryo can implant into the lining of the uterus (also known as the endometrium) and continues to develop into a fetus.

Luteal phase

After ovulation, the follicle that released the egg becomes the corpus luteum which produces progesterone to maintain the endometrium and support pregnancy if conception occurred.

5. LIFESTYLE FACTORS AFFECTING FERTILITY & PREGNANCY



Smoking

Smoking can be the cause of many fertility problems for both men and women. Women who smoke will have more difficulty conceiving, particularly during an IVF cycle, as the medication is less effective. Smoking can also cause an increased chance of early menopause and an increased risk of cervical and vulval cancer. There is also an increased risk of miscarriage, preterm delivery and low birth weight babies. Once a child is born, there is an increased risk of sudden infant death syndrome (SIDS) and feeding difficulties.

Smoking in men can affect the production of sperm (quality, count and volume can be reduced). There is also a higher risk of erectile dysfunction. Second hand smoking has been found to be as harmful to couples during conception and pregnancy as smoking first hand. A baby exposed to cigarette smoke during pregnancy (including passive smoking) is more likely to develop type 2 diabetes, heart disease, kidney disease and be obese as an adult. These risks are increased even if they are non-smokers throughout their lives. The above information is available from the Quit Now fact sheet - Smoking and Reproductive Health, available online: <http://www.quitnow.gov.au>.

Weight / BMI

At PIVET, we like patients to aim for a healthy BMI range of 20-26kg/M². If you are under or over weight, you may experience ovulation problems. Diabetes and polycystic ovarian syndrome (PCOS) can also influence weight gain and certain interventions can be discussed with your doctor. Often, once weight issues are addressed, your fertility outcomes can be drastically improved.

While we like patients to aim for the healthy BMI range, we will still allow treatment such as IVF to proceed with a BMI up to 35kg/M². You must be less than 35kg/M² and weigh less than 110kg to commence any treatment cycle.

BMI can be calculated by Weight (kg) / [Height (m) x Height (m)].

If you are having trouble achieving this goal please arrange to speak with one of the clinic nurses or with your doctor to discuss a weight loss management plan.



Diet & Exercise



It is advised that in the lead up to treatment, during treatment and during pregnancy that you consume a well-balanced diet. This includes consuming 2 serves of fruit and 5 serves of vegetables daily and including grain and lean proteins in your diet.

Try to reduce your consumption of refined sugars and drink plenty of water. Regular gentle exercise is important for general wellbeing, as well as for psychological wellbeing.

Walking, swimming, yoga and pilates are great ways to stay fit and healthy and also reduce stress levels. Be careful not to over exercise as this can have a negative affect on your hormone levels and menstruation.

Alcohol

The consumption of alcohol while planning and attempting conception can have a negative impact on your success. This is due to the effect alcohol can have on your body. Alcohol consumption can have direct and indirect effects on the brain, the pituitary gland (the part of the brain responsible for the secretion and regulation of hormones) and the ovaries and testes. Therefore it is advised in the lead up and during fertility treatment that both you and your partner abstain from the consumption of alcohol. For further information refer to <http://www.drinkwise.org.au/alcohol-pregnancy>.

Age

When females are born, they have about 400,000 antral follicles (immature eggs) stored in their ovaries. Women are most fertile following puberty, however these days many women wait until their 30s to begin their families. Unfortunately, even with improved health later in life, the natural age related decline in fertility cannot be prevented or reversed. As women age the number and quality of eggs that remain in the ovaries each month decline, particularly after the age of 35. Your doctor will discuss your chances of success with fertility treatment relevant to your age group.

6. PREPARING FOR TREATMENT

Multivitamins

It is advised that all patients take a multivitamin during the pre-conception stage and pregnancy. There are a range of multivitamin preparations on the market and it is up to you which preparation you decide to take.

Please speak to your doctor or nurse if you require more information on choosing the right multivitamin for you.

Folic Acid

Folic acid is a water soluble vitamin which is important for the body to build healthy cells. This is especially important when planning a pregnancy and during pregnancy. It is recommended that you commence taking folic acid 3 months prior to planning pregnancy and continue throughout your fertility treatment here at PIVET.

Folic acid is important during pregnancy as it reduces the chances of birth defects such as *spina bifida* in babies.

At PIVET, our Medical Director advises that all patients undergoing fertility treatment and pregnancy should be taking a daily dose of 5mg of folic acid.

This can be taken in conjunction with your regular prenatal multivitamin (which may also contain folic acid).

Vitamin D

During your initial investigations, your vitamin D levels will be tested. A large majority of patients are found now to have deficient levels which can have a negative impact of general wellbeing and also pregnancy and the developing baby.

Vitamin D is largely obtained from sunlight, however as we age our ability to convert sunlight to vitamin D decreases.

Vitamin D is important for bone and muscle health and our immune system. If you are found to be deficient at your initial blood test, it is advised you commence taking a daily dose of 1000IU Vitamin D.

Please discuss this further with nursing staff or your doctor if you have any concerns or questions.



7. COUNSELLING

PIVET Medical Centre and Perth Day Surgery Centre provide a comprehensive specialist counselling service for all patients before, during and, if necessary, at the conclusion of treatment. Our Counsellor is an RTC Approved (Fertility) Counsellor and practicing Clinical Psychologist. She has worked in the field of fertility for over 15 years and, as per the Reproductive Technology Council's requirements, works independently of the clinic.

Appointments with the Counsellor are available at PIVET during the week and on alternate Saturdays. When patients are not able to attend the clinic due to distance or circumstance, Skype appointments may be possible.



Pre-treatment Counselling

A counselling session prior to commencing fertility treatment is strongly recommended. This is largely an educational session and focuses on the common stressors associated with treatment and assists patients to identify effective coping strategies and address any other concerns they have prior to commencing treatment. All patients proceeding to IVF treatment are entitled to a counselling session free of charge.

Other Counselling

Crisis, support or therapeutic counselling is available to assist patients address other fertility related difficulties including anxiety, depression, relationship distress and grief and loss. Patients may request this service themselves and arrange an appointment through PIVET's reception or they may discuss their needs with their doctor or a clinic nurse. There is a fee for this service, but patients may be eligible for a rebate from their private health insurer, if they have the appropriate ancillary cover, or from Medicare if they have a Mental Health Treatment Plan and a referral from their GP. A list of other Approved Counsellors is available on the Reproductive Technology Council's website: www.rtc.org.au.

Donor Issues Counselling

Treatment involving the donation of sperm, eggs or embryos between persons known to each other requires counselling for each party before the RTC mandated "cooling off" period commence, and again at the conclusion of the "cooling off" period. This is an RTC requirement.

With respect to the unknown donation of sperm, eggs or embryos, PIVET requires all donors and recipients to meet with the counsellor to consider the personal, familial, legal and social implications of donating or receiving donated gametes or embryos, and the needs of the donor conceived child, prior to commencing treatment.

Genetic Counselling

Genetic counselling is available to patients who may have an inherited disorder in their family, patients wishing to have Pre-implantation Genetic Diagnosis, donors and recipients in our donor program and patients wanting additional information on inherited factors. Genetic counselling is available from the Genetic Counsellor who consults to PIVET.

SUPPORT GROUPS

Access Australia - www.access.org.au

Australian Infertility Support Group - <http://www.nor.com.au/community/aisg/infertilitylinks.htm>

Donor Conception Support Group - <http://www.dcs.org.au>

***All counselling appointments can be made with our Reception staff.
Fees apply (except in the case of pre-IVF counselling).***

8. TRACKING WITH TIMED INTERCOURSE

In some situations couples may only require limited intervention and therefore may be offered cycle tracking with timed intercourse. This involves accurately determining the time of ovulation for the female. This cycle is similar to an assessment cycle with the exception of the HyCoSy procedure (see the above section for more information on assessment cycle and HyCoSy).

Hormone levels are measured on Day 2 and then second-daily with ultrasound scans from Day 8 or 9 of the cycle to track the growth of follicles, which will establish the optimum time of ovulation. Once an adequate response is observed, you will be advised by nursing staff when the appropriate timing for intercourse is in relation to ovulation. You may be given the opportunity to attend the clinic for a post coital test to assess sperm / mucous interaction during the cycle.

After timed intercourse has occurred, a mid-luteal blood test approximately 9 days later will be performed to check the level of support hormones (oestrogen and progesterone) to determine if these levels are sufficient to support pregnancy.

In some circumstances extra support medication, usually in the form of vaginal pessaries, will be commenced to provide optimal hormone levels to aid conception.

A pregnancy test will be performed 10 days following the mid-luteal blood test if support medication has been commenced. If no support medication has been prescribed patients are advised to contact the clinic if their period is late to check for pregnancy.



9. OVULATION INDUCTION

Ovulation induction (OI) involves the use of low-dose hormones to induce ovulation in patients whose own ovulation process may not be satisfactory. Ovulation induction involves hormonal stimulation of the ovaries. Hormone stimulation will assist in the production and release of eggs. It will also further improve the embryo's chance of implanting successfully in the lining of the uterus. Hormone blood testing and ultrasound scanning will be conducted in a similar fashion as discussed in the timed intercourse treatment program above.

Consents

Prior to commencing any treatment cycle involving the use of medications you will be required to sign the appropriate consent forms. Consent forms are to be completed at your Day 21 appointment or at the latest, prior to commencing your treatment on Day 2. Consents are retained in your patient file at PIVET. **PIVET has a strict "No Consent = No treatment" Policy.**

A typical OI cycle involves phoning PIVET on the first day of your period to let us know you are ready to start your cycle (*if your period commences after midday, the following day is considered as Day 1*).

On Day 2 a blood test will be performed between 7.30 and 9.30 am (Monday – Friday) at PIVET, to assess your baseline hormone levels before stimulation commences. After every test you will be contacted by one of the nurses with your results. If your doctor has prescribed Tamoxifen or Clomid, commence this on Day 2 as directed.

From Day 8 or 9 you will be required to attend the clinic for blood tests and ultrasounds which continue second daily until ovulation occurs. Please abstain from intercourse until given further notice. A full bladder is not required for your ultrasounds as this is performed trans-vaginally. The ultrasound is to monitor developing follicles/egg(s) and to assess the thickness and quality of your endometrium (the lining of the uterus).



conception and pregnancy.

Some patients may develop more than three (3) mature follicles in response to the medication. The chance of a multiple pregnancy occurring in such a cycle is quite high, which may be detrimental to both mother and babies. We may therefore cease further treatment in the current cycle and you will be booked in to see a PIVET doctor to discuss this further.

When the test results indicate ovulation is approaching, you may be instructed to use a hCG injection (Ovidrel or Pregnyl) to trigger ovulation. Once you take the trigger, STOP your medication if you have not finished it already. You will then be required to have intercourse for the following 3 days. You may require luteal support during the second part of your cycle. This will be discussed with you by your doctor and the clinic nurses. You will be given a timetable to follow outlining the support medications and blood test requirements. Usually vaginal pessaries or hCG injections are given until the final pregnancy test to support

A mid-luteal blood test is performed approximately 9 days after “trigger” to check the level of support hormones (oestrogen and progesterone) to determine if they are sufficient to support pregnancy. In some circumstances extra support medication will be commenced to provide optimal hormone levels to aid conception. A pregnancy test will be performed 10 days following the mid-luteal blood test.

10. INTRA-UTERINE INSEMINATION

Intra-uterine insemination (IUI) is available when the male partner (in the case of heterosexual couples) is producing sufficient sperm for fertilisation but for some reason, the sperm are not able to penetrate the cervical mucus and thus reach the uterus and fallopian tubes where fertilisation normally occurs. This problem is usually diagnosed by a post-coital test (PCT) where the sperm-mucus interaction is examined the morning after intercourse at the appropriate time of the cycle. If the sperm has not penetrated through the mucus this suggests “cervical hostility”, a rather poorly defined condition where abnormal mucus forms in the cervix. Same sex couples may also access IUI utilising donor sperm.

IUI is also carried out when there are problems with high semen viscosity preventing the sperm from swimming out of the seminal plasma. In addition there are a number of male medical problems in which IUI may be indicated (e.g. some forms of impotence and ejaculatory failure). In order to overcome the problem of sperm-mucus penetration, semen is put through a special wash and preparation to separate out the most motile sperm. The sperm is then placed directly into the uterus bypassing the hostile mucous.



It is important to abstain from sexual intercourse / ejaculation from Day 8 of the treatment cycle. This will allow for adequate development of sperm in the sample used for the IUI procedure.

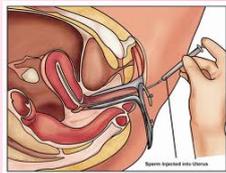
Consents

Prior to commencing any treatment cycle at PIVET you will be required to sign the appropriate consent forms. Consent forms are to be completed at your Day 21 appointment or at the latest prior to commencing your treatment on Day 2. Consents are retained in your patient file at PIVET. **PIVET has a strict “No Consent - No treatment” Policy.** A typical IUI cycle involves phoning PIVET on the first day of your period to let us know you are starting your cycle (if your period commences after midday, the following day is classed as Day 1). On Day 2 a blood test will be performed between 7.30am and 9.30am (Monday – Friday) at PIVET to assess your baseline hormone levels before stimulation commences. After every test you will be contacted by one of the nurses with your results. If your doctor has prescribed Tamoxifen or Clomid, commence this on Day 2 as directed.

From Day 8 or 9 you will be required to attend the clinic for blood tests and ultrasounds which continue second daily until ovulation is predicted. A full bladder is not required for your ultrasounds as they are performed trans-vaginally. You will be asked to empty your bladder prior to your scan. The ultrasounds are to monitor developing follicles/egg(s) and to assess the thickness and quality of your endometrium (the lining of the uterus).

Some patients may develop more than three (3) mature follicles in response to the medication. The chance of a multiple pregnancy occurring in such a cycle is quite high, which may be detrimental to both mother and babies. We may therefore cease further treatment in the current cycle and you will be booked in to see a PIVET doctor to discuss this further.

When the test results indicate ovulation is approaching, you will be instructed to use a hCG injection (Ovidrel or Pregnyl) at a set time to trigger ovulation. Once you take the trigger injection, STOP your medication if you have not finished it already. Your IUI procedure is then timed for 42hrs post-trigger injection.



IUI Procedure

You will be required to attend Perth Day Surgery Centre (co-located at PIVET) for the IUI procedure.

Sample collection

On the day of your IUI, your partner (in the case of heterosexual couples) will be asked to produce a semen specimen, in the PIVET collection room, 1 - 2 hours prior to the procedure, so the laboratory staff have enough time to prepare the sample. This involves the semen being washed and the most motile sperm cells collected. If donor or frozen sperm is to be used, it will be prepared for your appointment time.

Sample Preparation

1. The solution used for the semen preparation for the IUI procedure contains a protein of human origin (HSA) that it has been screened for infectious diseases. The protein (HSA) has been used in media for many years and is approved by the Therapeutic Goods Authority (TGA).
2. If you do not want to use human blood products, the use of synthetic protein is possible. It is however costly (the cost is currently in excess of \$1000.00).

At the time of insemination, a small catheter is passed through the cervix under ultrasound guidance into the uterus where the sperm are introduced. It is a painless procedure taking about 5 minutes, and you will be required to lie down for 30 minutes afterwards.

The IUI procedure has minimal side effects associated with it. Relatively few women have any discomfort during the procedure. Approximately 2% have uterine cramping and associated nausea, which can be relieved by an injection to relax the muscles and reduce nausea. After the procedure, a mid-luteal blood test will be performed 9 days later to check the level of support hormones (oestrogen and progesterone) to determine if these levels are sufficient to support pregnancy.

In some circumstances extra support medication will be commenced to provide optimal hormone levels to aid conception. A pregnancy test will be performed 10 days following the mid-luteal blood test.

11. MEDICATIONS USED DURING MINIMAL INTERVENTION

TAMOXIFEN

Tamoxifen is usually prescribed to women who cannot tolerate Clomid. Tamoxifen is an anti oestrogen drug and it is generally considered to increase fertility rates similar to Clomid. Commence with 20mg daily from day 2 – 10 unless prescribed otherwise.

Tamoxifen should not be given to women with a personal or family history of blood clots or to women who are known to have genetic defects that predispose them to thrombophilia. Please inform your doctor if you have any of the above.

Side Effects

Stomach and bowel upsets, hot flushes, bloating, headache, dizziness, depression and breast discomfort. Multiple pregnancy is a risk whenever ovulation is induced with fertility drugs.



HCG (PREGNYL / OVIDREL)

This drug is used to mature the eggs and trigger ovulation during an IVF cycle and is sometimes used to support the early stages of a pregnancy following the transfer of an embryo during an IVF cycle. The injection aids the corpus luteum (the remains of the follicle once the egg is released / collected at TVOA) in the production of progesterone, required to prepare the uterine lining for implantation of an embryo.

Ovidrel or Pregnyl may be prescribed in different doses depending on your response throughout your cycle and also depending on what type of cycle you have undertaken. The nursing staff will inform you of the dose and frequency that the doctor has prescribed for you. This will be written on your discharge paperwork also.

Possible Side Effects

Breast tenderness and/or enlargement, ovarian tenderness, abdominal distention – bloating, nausea and constipation, pain at the injection site and headaches.

COMBINATION PESSARIES (OESTROGEN / PROGESTERONE)

The doctor may have prescribed combination pessaries, which act in the same manner as the progesterone pessaries, with a small amount of oestrogen for added support if indicated by your hormone levels.

BUYING PESSARIES

Pessaries are made to order in a compounding pharmacy. We recommend our patients to use **Wembley Pharmacy** (361 Cambridge Street, Wembley, Perth, WA 6014 ☎ 08 9387 3079) or **Usher Pharmacy** for South West patients (36 Cranbrook Way, Bunbury, WA 6230 ☎ 08 9795 7631).

PROGESTERONE PESSARIES

Progesterone is a hormone essential for establishing and maintaining pregnancy. You may be prescribed progesterone pessaries in order to supplement your body's own production of the hormone. The hormone will help prepare your uterus to receive and maintain an embryo. If pregnancy occurs, pessaries must continue until approximately 10 - 12 weeks of pregnancy, which is when production of progesterone by the placenta is adequate.

Pessaries should be inserted high into the vagina and the patient should rest, lying flat, for 30 mins after insertion to aid in the absorption of the hormone. A small amount of white, waxy discharge will be present afterwards - this is the base material in which the hormone is suspended and will not be absorbed by the body. In certain circumstances, you may be instructed to take the pessaries rectally.

A nurse will provide you with further instructions if this is the case.

No adverse effects have been reported when progesterone pessaries are used in this manner.

12. RISK OF MULTIPLE PREGNANCY IN MINIMAL INTERVENTION TREATMENT

PIVET Medical Centre is committed to assisting patients to achieve a singleton pregnancy (one baby), as multiple pregnancies present significant medical risks for babies and mothers; and the psychosocial impact on parents and children are also significant.

Fertility treatment, including Intrauterine Insemination (IUI), carries a higher risk of multiple pregnancy as a result of the drugs used for ovarian stimulation.

Your individual success rate on this treatment will depend on your age, underlying disorders or pathology and your partner's sperm count and quality.

When preparing for fertility treatment, a doctor will discuss with you the likelihood of multiple pregnancy that your treatment may pose.

**PLEASE ALSO REFER TO SECTION:
RISKS, SIDE EFFECTS AND OTHER CONSEQUENCES OF
ASSISTED REPRODUCTIVE TECHNOLOGY**



IVF TREATMENT CYCLE

1. WHO IS SUITABLE

The following cases are most likely to benefit from IVF:

- ★ Blocked or damaged fallopian tubes.
- ★ Couples where the male partner is oligospermic (low sperm count), especially where there is poor sperm motility.
- ★ Anti-sperm antibodies (ASAB's) - these can interfere with the normal mode of fertilisation.
- ★ Couples with unexplained infertility, where it is desirable to confirm that fertilisation is occurring.
- ★ Endometriosis.
- ★ Polycystic ovarian syndrome.
- ★ Single or de facto women with proven infertility.
- ★ Anonymous egg donation.



2. PRE TREATMENT CONSULTATION

Before you start an IVF treatment cycle, you will need to see a Fertility Specialist at PIVET.

It is recommended that you telephone the clinic on Day 1 of the cycle prior to undertaking IVF to arrange this appointment.

We refer to this as your “Day 21” appointment



During this consultation, your doctor will, among other things, review your treatment options and management and ask you and your partner to read, understand, ask questions on aspects you need further information or clarification on and then sign the consent form(s).

Consent forms are to be completed at your Day 21 appointment or at the latest prior to commencing your treatment on Day 2. Consents are retained in your patient file at PIVET.

A transvaginal ultrasound will need to be performed around day 21 of your cycle. You will be given a referral to attend this at an outside provider either prior to or following your Doctor appointment. This ultrasound is to exclude ovarian cysts and any other abnormalities that may affect your treatment outcome. During the consultation, vaginal swabs will be taken to exclude infection.

You should have received advice from the accounts staff on the costs of the proposed treatment cycle and be clear on how the costs are managed between your health fund, Medicare and yourself.

This will vary between cycles depending on many factors including which health fund you are a member of and previous treatments in the current calendar year.

3. REGIME TYPES - SUPPRESSION OF THE NATURAL HORMONES & STIMULATION OF THE OVARIES

The types of regimes that we offer include:

- **FLARE** or **LONG DOWN REGULATION** - see below.
- **ANTAGONIST REGIME** - see below.
- **AACEP REGIMEN**
The AACEP (Agonist / Antagonist Conversion with Estrogen Priming) is a new protocol primarily for poor responders. It involves the sequential administration of several medications in the cycle before an IVF attempt and during the cycle. Your clinician will explain the regimen in more detail during your consultation.
- **NO PITUITARY DESENSITISATION**
- **NATURAL OR LOW DOSE STIMULATION CYCLES**
There may be a number of reasons when a natural or low dose stimulation cycle may be offered as a treatment regime. Some women have ovaries that do not respond well to stimulation. Others may have improved egg quality when no or low dose stimulation is used. Finally, women who have had side effects to ovarian stimulation may benefit from these regimes.



Routinely at the commencement of the menstrual cycle the body produces hormones to allow an egg to grow. In the IVF procedure we stimulate the ovaries to produce more eggs, and in order to do this we need to suppress the natural cycle.

This can be achieved using a group of drugs known as GnRH agonists and antagonists. Lucrin and Syneral are the *agonist* drugs used at PIVET and they act to “desensitise” the pituitary gland, so that we can have better control over your ovarian stimulation. This will prevent your follicles from ovulating prior to the eggs being collected. These regimes are referred to as **FLARE** or **LONG DOWN REGULATION** cycles, depending on the timing of when you are to commence then drug.

Cetrotide and Orgalutran are the *antagonist* drugs used at PIVET and they work directly on the pituitary gland during an **ANTAGONIST** regime. It is normally administered several days prior to ovulation to prevent the follicles from spontaneously rupturing and releasing their eggs.

Follicular growth in the ovaries is stimulated by injections of a synthetic form of FSH (Follicle Stimulating Hormone), mimicking what is normally produced by the pituitary gland of the body. In the IVF cycle we monitor the amount of follicles we produce and adjust the dose of FSH accordingly. This is important as too high a dose of FSH can cause Ovarian Hyper Stimulation Syndrome (OHSS) (see Section 17 for further information on OHSS). FSH is used in all types of cycles (excluding Natural IVF cycles) in addition to the agonist or antagonist drug. Types of FSH injections used at PIVET include Gonal-F, Puregon, Elonva and Menopur.

The progress of the cycle is monitored by checking hormone levels through blood tests and ultrasounds for follicle tracking. Ultrasounds for follicle tracking are performed trans-vaginally in our ultrasound department. The ultrasound scan is performed to measure follicle size, development and quantity. For this scan, an empty bladder is required.

A blood test is routinely performed on Day 2 to check that hormone levels are baseline. You will receive an email in the afternoon, instructing you on starting your drugs. If you have any queries from the email that you receive please phone Pivet to speak to one of the nursing staff. They are then checked again, along with an ultrasound scan, at Day 6 - 9, depending of which type of stimulation regime you are undergoing. This ensures adequate oestrogen is available to support follicular growth. We may also commence your antagonist drug at this stage (if applicable).

Thereafter, second-daily blood tests and ultrasounds are performed to monitor the hormone levels and growth of the follicles. The dose of FSH can be adjusted if follicular response is inadequate. The follicle is a fluid filled sac in which the egg develops. Growth of follicles to maturity generally takes about 10 - 12 days and they usually measure 18 - 25 millimetres in diameter at the time of ovulation. The egg (or ovum) measures about 1/10 of a millimetre within the sac.

4. TRIGGER INJECTION

When your follicles are of sufficient maturity and size, your Fertility Specialist will order a trigger injection. This injection mimics the natural surge of LH at ovulation. There are several variations in trigger injections at PIVET and this is largely organised during the consultation and then a final decision is made at the results meeting after taking into account your follicle numbers and hormone levels.

It is important to follow the instructions given by the nursing staff exactly, as deviations may influence the number of oocytes we recover at egg collection. After your trigger injection you will be required to stop most of your other injections as instructed by the nurses.

5. EMBRYOLOGY APPOINTMENT

All patients who are undertaking an IVF or a FET cycle must meet with an embryologist prior to egg collection or embryo transfer day. Usually the appointment is set up for after your second ultrasound scan at PIVET. Bookings to see the embryologist are made through the nursing department.

An embryologist will go through your treatment cycle in depth, explain to you the many different facets of the laboratory work and outline the plan for your individual treatment. This appointment will allow you the opportunity to ask any questions regarding your treatment, so you understand the procedures the laboratory will undertake during your treatment cycle.



6. COLLECTION OF EGGS (OOCYTES) & SPERM



Eggs (brown spot) seen at collection surrounded by cumulus

Collection of Eggs

You may have heard of us referring to this as your egg retrieval, egg collection or TVOA (Transvaginal Oocyte Aspiration). After you are administered a Neurolept (Twilight) anaesthetic, a vaginal ultrasound is performed allowing your ovaries to be visualised. Attached to the vaginal ultrasound probe is a needle guide through which a fine needle is passed through the vaginal wall into the ovaries containing the follicles.

Each follicle greater than ~10 millimetres is then needled, and its contents (follicular fluid) aspirated into a test tube. The test tube and its contents are handed to an embryologist to check for the egg. This is repeated until all follicles have been aspirated. The process takes approximately 30 minutes.

The aim is to collect an egg from every follicle. Occasionally eggs will not be found in some follicles and on rare occasions, no eggs will be recovered during the procedure, resulting in a failed egg collection. Sometimes the eggs that are collected can be immature and therefore not ready to receive sperm for fertilisation. If this does occur, your doctor will assess your treatment regimen on your next consultation in an attempt to improve follicle numbers and/or oocyte quality.

After the collection, the eggs are washed and placed into a dish containing culture media. In the meantime the sperm sample would have been produced and then prepared (see below).

Risks and complications are very rare, but may include:



- Infection
- Moderate to severe discomfort
- Twisted ovary (ovarian torsion)
- Perforation of the bladder, bowel or blood vessels
- Heavier than usual vaginal blood loss
- Bleeding from the ovary
- Anaesthetic complications

Collection of Sperm

At an arranged time, your partner will be asked to produce a semen sample that will be analysed, prepared and washed to isolate the most motile, normal sperm. Please ensure you abstain from sexual activity for 2-7 days prior to the egg collection day.

Do not abstain for longer than 7 days. This will build up the number of poor quality sperm in your sample which can effect the healthy sperm (see section on semen preparation).

Alternatively, donor sperm (frozen), frozen partner sperm or surgically collected samples (where required) are prepared by the laboratory on the day of egg collection.

When your partner is given a time for egg collection, we will also notify the time you are required to produce your sample on the same day.

Providing a semen sample can be an embarrassing and stressful experience. We will attempt to make this event as easy as possible for you.

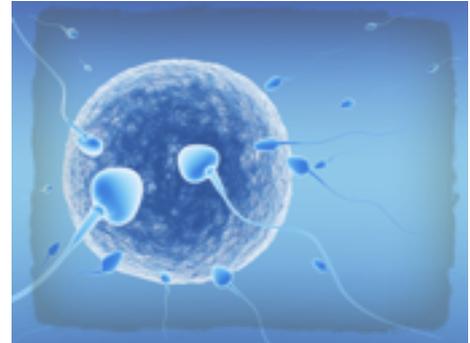
- If possible, take a shower before you come to PIVET to produce your specimen. Ensure that all soap has been rinsed off.
- Please wash your hands with soap and water, and rinse thoroughly before producing your sample.
- Do not use any lubricant or condoms as this will damage the sperm.
- Collect the whole specimen into the sterile container provided. Ensure you write your **name, date of birth, address** and time of collection on the jar.
- Complete the semen collection sheet provided in the collection rooms, filling in all the required information. If you have any further information that you think may be necessary, please write it down as well.
- Place the sample, request form and semen collection sheet in the hatch on the wall, close the hatch (unless you wish to speak to the laboratory staff) and press the buzzer to notify the laboratory that

there is a specimen to collect.

Although we would prefer the sample to be produced at the clinic, it may be produced off premises and brought into the clinic provided the time to travel is within one hour. If you must collect the specimen at home or away from PIVET premises, you can collect a sterile sample container from one of our staff. Please make sure your **name, date of birth, address** and time of collection are on the container and the semen collection form is completed and handed in with the sperm sample.

These are our preferred methods. However if you foresee a problem with the above procedures, please discuss with your clinician for alternate collection information. If you cannot produce a specimen, do not worry. You can always try later, however please discuss this with the laboratory staff so they may change the schedule.

The PIVET Andrology Laboratory can also cryopreserve (freeze) your semen prior to your partner's treatment cycle so you will not have to produce a sample on the day of egg collection. Due to the freezing process there may be a reduction in sperm quality, so 2 or 3 samples may be required. If freezing is required please arrange to do this at least 3 weeks before your partner's egg collection. Fees apply for sperm storage (billed yearly). Unfortunately not all semen freezes well, and this procedure may not be suitable for you. Please inform the nursing staff if you wish to freeze your sperm. If your specimen is needed for an IVF related procedure, or insemination attempt, it will take 1 or 2 hours to prepare.



7. FERTILISATION - IVF & ICSI

There are two techniques the laboratory can use to fertilise the eggs collected. One technique is standard IVF and the other is intracytoplasmic sperm injection (ICSI). Sometimes a combination of the two methods will be used and this is known as an IVF/ICSI Split. Half the collected eggs will undergo standard IVF and the other half ICSI.

The type of insemination that will be performed will be discussed with you at your pre-treatment consultation. If your sperm profile indicates there are many sperm with strong motility and good morphology, your doctor may recommend standard IVF (see below) or an IVF/ICSI Split. If however, there are indications that standard IVF may place fertilisation at risk or if you are likely to produce only a few eggs then your doctor may recommend ICSI.

Each sample produced for standard IVF is checked prior to insemination and if found to be of either poor morphology or motility, the method of insemination may be changed from standard IVF to ICSI. This will only be carried out if you have given signed approval to do so in the consent form.

Following their collection, the eggs are transferred to the specially designed embryo culture laboratory. The eggs are evaluated for quality and placed in an incubator in culture medium containing commercially available human serum albumin (HSA).



**The HSA is a human blood product and has been tested to support embryo development in vitro.
If you are concerned about its use, you have 1 further options:**

**The use of a commercial preparation of synthetic albumin that has been produced
by recombinant technology (cell culture production).
Please enquire about costings for this as it currently quite expensive.**

Three to four hours following the egg collection, the eggs will be inseminated according to your instructions marked on the consent form. The oocytes can be fertilised by standard IVF or by ICSI. Currently at PIVET the majority of oocytes are inseminated by ICSI.

Standard IVF

Standard IVF insemination involves the addition of a defined number of motile sperm to a dish containing the eggs. The fertilisation process takes place in the dish is thought to be similar to the process that occurs naturally, except it is outside the body. Standard IVF is performed when the male sperm count is exceptionally good and when greater than 4 mature oocytes are collected. The sperm must be particularly good as they must be able to fertilise the egg without any assistance.

If there are problems with the sperm, fertilisation of the eggs may be compromised. Your clinician in consultation with the embryologist will determine if standard IVF is a suitable form of treatment for you.

ICSI

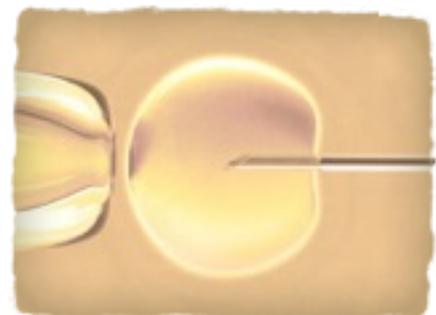
General Information

ICSI is a technique for the treatment for male infertility. The ICSI procedure is performed in the laboratory and involves taking a single sperm and injecting it with a glass needle into a mature egg.

Indications for ICSI

ICSI may be recommended by your doctor when:

- The sperm profile suggests a suboptimal capacity for fertilisation either by a low sperm count, reduced sperm quality or previous failed fertilisation.
- Less than 5 mature oocytes are expected to be collected.
- If using frozen sperm, and the sperm sample does not survive well when thawed.
- If you are using frozen sperm, and the thawed sperm sample is expected to have a reduced potential for fertilisation.
- The sperm has been surgically collected.
- A high level of anti-sperm antibodies are present.
- PGD (pre-implantation genetic diagnosis) or PGS (pre-implantation genetic screening) is to be performed.



Possible Risks Involved

- Following the egg collection, the embryologist will check the eggs to ensure they are mature and suitable for ICSI. Only those eggs that are mature can be injected with sperm. Approximately 30% of eggs are found to be immature, and therefore cannot be used for ICSI.
- Some eggs (4% at PIVET in 2019) do not survive the ICSI process.
- The overall fertilisation rate for those eggs injected using the ICSI technique was 74% (PIVET 2019). However, fertilisation for sperm retrieved surgically from the epididymis was 72% and from the testis 63% (PIVET 2019). On rare occasions, fertilisation does not occur following ICSI.
- Numerous published studies report that the incidence of abnormalities in foetuses and children from ICSI are no greater than IVF. Current information also suggests that the growth and development of ICSI children is similar to naturally conceived children. However there is a risk that some male infertility problems may be passed on.

- Monitoring of the pregnancy is offered to PIVET patients to assess abnormalities in the developing baby however, these procedures are not capable of detecting all abnormalities. PIVET can therefore not guarantee that any child born as a result of ICSI will be free of genetic or other abnormality.
- ICSI has so far resulted in over several thousand pregnancies worldwide. PIVET's own data published in 2018, showed the risk of significant congenital abnormalities in babies generated from ICSI created embryos is low at around 1.9%. Of the 415 babies born through ICSI generated embryos, there were only 8 significant congenital abnormalities from data collected between 2014 and 2017.
- Unfortunately, not all pregnancies will result in a baby. Miscarriage most frequently occurs very early in the pregnancy. PIVET will monitor the early stages of the pregnancy (first 8 weeks) closely via blood tests and ultrasound scans.

Fertilisation Check

Following standard IVF or ICSI the eggs are checked the next day for evidence of fertilisation, which is the presence of two pronuclei within the egg: one from the sperm and one from the egg. When these pronuclei breakdown, about 24 hours after sperm entry, the process of fertilisation is complete.

You will be informed of the outcome of the fertilisation check on the day following insemination, and providing fertilisation has been successful, the embryos will be transferred either 48 hrs (Day 2), 72 hours (Day 3), 96 hours (Day 4) or 120 hours (Day 5) after egg collection. The eggs cannot be re-inseminated if we suspect problems with fertilisation prior to transfer.



It is important to understand that, like in nature, fertilisation does not always occur. This can be due to either egg or sperm factors, or both, and is usually difficult to diagnose. The average fertilisation rate is similar between IVF and ICSI at 65 - 74% with failed fertilisation being a rare event. If there are only 1 - 2 oocytes, no fertilisation may occur by chance, due to the low number of eggs. This is one reason why PIVET recommends ICSI for cases involving low oocytes numbers.

IVF/ICSI Split

An IVF/ICSI Split involves a certain number of your collected eggs put to standard IVF fertilisation and the rest to ICSI fertilisation. The number committed to each fertilisation type can be decided with your Clinician. The reason behind performing split cases is to avoid any cases of unexplained failed fertilisation, which happens when no eggs fertilise and no reason can be identified as to why. As fertilisation through standard IVF is a complex process which involves the binding and incorporation of sperm into the egg, if any step of the process fails, the egg will not fertilise. Sometimes it is impossible to predict if this going to happen, as both the eggs and sperm look normal. ICSI bypasses many of the steps in normal fertilisation as the scientist does most of the work for the sperm and egg by depositing the sperm directly into the egg. In most cases if there is no fertilisation with standard IVF, you will get fertilisation with ICSI.

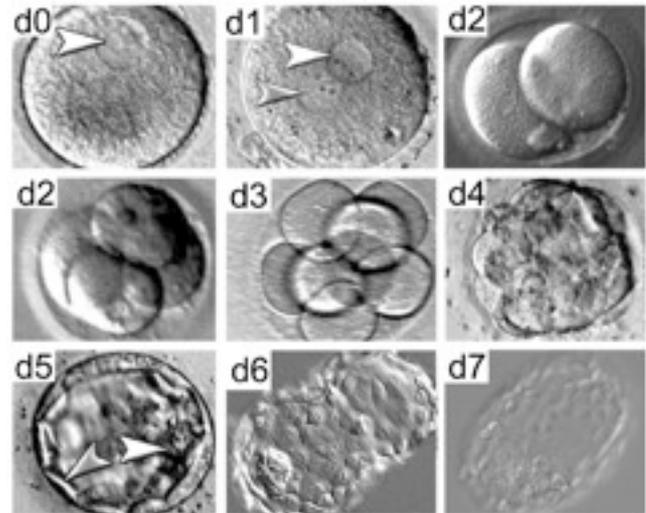
Your clinician may decide to offer you a split fertilisation so that if the standard IVF fertilisation fails, you will still have a chance that the ICSI eggs will fertilise and be available for use in your treatment cycle. If you get fertilisation with both standard IVF and ICSI, you may opt to have the embryo from your desired method of fertilisation transferred. All resulting embryos are tracked, therefore we will know which eggs have undergone IVF and which ones have undergone ICSI.

8. CULTURING OF EMBRYOS

PIVET Medical Centre utilises a commercial solution to grow embryos. Solutions for fertilisation, early division of the embryo and blastocyst have been developed with different formulations for each of the embryo growth stages.

With this new culture system, the embryos can be kept in the incubator for a longer period until they reach a more advanced growth stage referred to as blastocyst.

During your treatment cycle, fertilisation will be achieved in specially formulated fertilisation solution. They will remain in this solution from Day 0 (the day of egg collection) to Day 1 (day of fertilisation check). The embryos will then be placed in cleavage solution for 1 day until Day 2 or 2 days until Day 3.



On Day 2 the embryos should have developed to 2-4 cells or by Day 3 to 6 - 8 cells. A Day 2 or Day 3 stage embryo may be transferred into the uterus.

If the transfer does not go ahead on Day 2 or Day 3, the embryos will be placed into blastocyst solution on Day 3 until Day 4 or Day 5 for embryo transfer. The embryos will be transferred back into the uterus on either Day 4 or Day 5. Day 4 embryos are either morula's, compacting, cavitating or early blastocysts, and Day 5 embryos should be blastocysts. Current reports show that approximately 50% of good quality Day 3 embryos will develop to blastocysts. At PIVET, there is no difference in the pregnancy rate between Day 4 & Day 5 embryos. Good quality blastocysts not transferred in this cycle may be cryopreserved (frozen).

Since 2008, PIVET has had a variable embryo transfer policy. Patients with 4 or more fertilised embryos will have a Day 4 or Day 5 embryo transfer, while those with less than 4 fertilised embryos, will have a Day 2 or Day 3 embryo transfer.

Blastocyst culture is used at PIVET as an embryo selection tool. If a patient has a large number of good quality Day 2 or 3 embryos, it becomes a challenge for the embryologists to identify the embryo that will give you the highest chance at pregnancy. By culturing another 1 or 2 days to morula or blastocyst, you will find that some embryos continue to developed while others will stop dividing or arrest. This will allow the identification of the embryo which will give you the highest chance of a pregnancy.



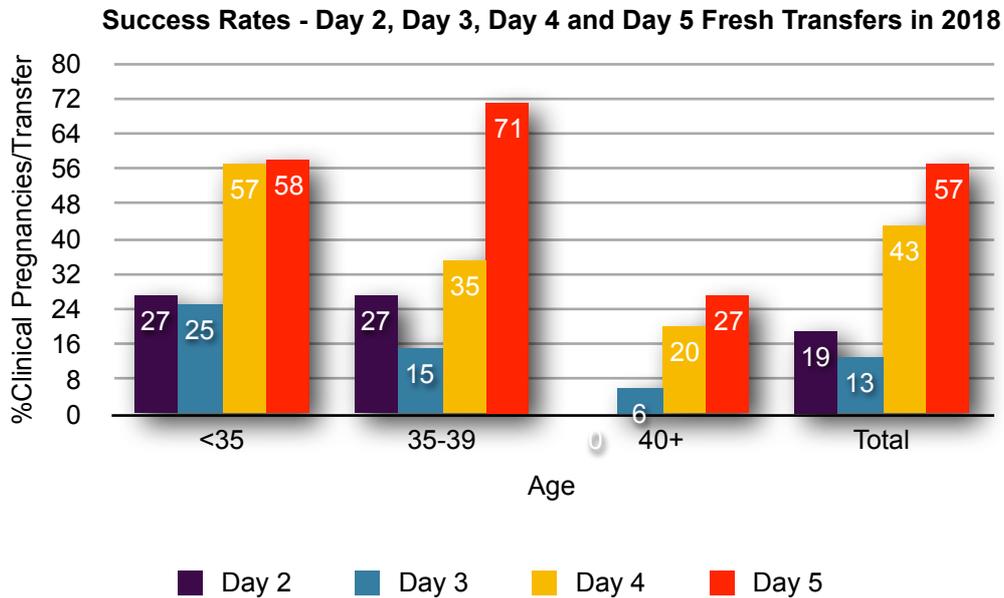
With a small number of fertilised eggs, there is a risk that no blastocysts will develop and therefore we will be unable to perform an embryo transfer. With smaller embryo numbers, it is also easier to select the best embryo for transfer. Therefore, when you have smaller embryo numbers, we will perform a transfer on Day 2 or 3.

PIVET data in 2018 showed 41% of embryos cultured to Day 5 or 6 developed into a blastocyst of a suitable quality to transfer or freeze. The PIVET pregnancy rate for transferred blastocysts was 57% for all ages in 2018 as illustrated in the graph below.

The transfer of an embryo at the blastocyst stage appears to increase the monozygotic (identical) twinning rate. This may be due to the embryo splitting as the blastocyst breaks out the "egg shell" or zona. A study conducted by Rijnders et al (1998) reported a rate of 2.3% monozygotic twinning following blastocyst transfer, compared to 0.41% for day 2 transfers. By reducing the number of embryos transferred, the risk of multiple pregnancy is minimised.

Our policy is to encourage "Single Embryo Transfer" (SET) for all women under 40 years of age to minimise the chances of multiply pregnancies.

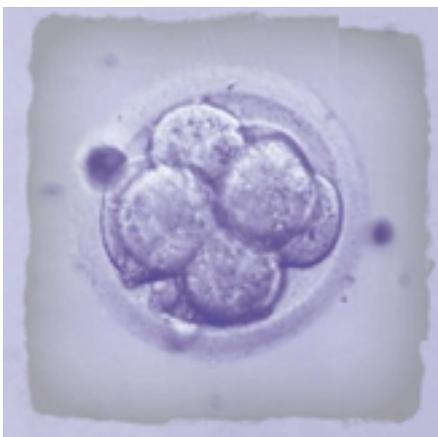
There are risks involved both to the mother and babies with multiple pregnancy and these are normally discussed with you at your consultation with the clinician.



9. EMBRYO TRANSFER

The embryo transfer procedure is performed in Perth Day Surgery Centre. Most embryo transfer procedures do not require an anaesthetic. The procedure involves placing a speculum in the vagina followed by insertion of a fine tube into the womb under ultrasound guidance. A second tube loaded with the embryo is then passed through the first and the embryo is expelled into the uterus. You will be able to see this process happening on the ultrasound screen.

The procedure takes about 10 minutes and is usually much like having a pap smear. You will be asked to rest for 30 minutes afterwards before going home. If you experience increased levels of discomfort during the procedure, subsequent embryo transfers may be performed with valium or anaesthesia. This should be discussed with your doctor. Risks and complications are very rare, but may include: infection, mild irritation of the cervix, slight bleeding from the cervix, minor discomfort.



Following the embryo transfer, your hormone levels and general well-being will be monitored closely. Your regime may be altered depending on these factors to optimise your chances of pregnancy.

See section “Luteal Support” for further information.

Additional hormone support will be initiated if required. **DO NOT CEASE OR CHANGE ANY MEDICATION UNLESS YOU ARE INSTRUCTED TO DO SO.**

If you cease support medication prematurely, this can severely affect your outcome.

In the unfortunate event of failed fertilisation or failed embryo development, you will be given Provera (a synthetic progesterone) to ensure you will get your period.

Questions following embryo transfer – refer to section on post-transfer in the Day Surgery (PDSC) section.

10. EMBRYO FREEZING

If more good quality embryos develop than is required for the fresh embryo transfer, you may choose to have these frozen (cryopreserved).

Embryo freezing is performed if:

- There are excess viable “good quality” embryos (embryos that have reached the required cell stage, with minimal fragmentation or other abnormalities) after fresh embryo transfer. At PIVET, all excess embryos are cultured to Day 6, and if “good quality” blastocysts develop, they will be vitrified (frozen). Every embryo is given a chance to show its potential before being allowed to succumb.
- Problems with the uterine environment, such as polyps or fibroids, make a fresh embryo transfer undesirable.
- Problems with your hormone levels reducing the chance of pregnancy.
- A medical condition such as Ovarian Hyperstimulation (OHSS) prevents a safe embryo transfer.



If pregnancy does not ensue from your fresh embryo transfer and there have been excess embryos frozen for you, a frozen embryo transfer (FET) cycle is recommended prior to another fresh stimulated cycle.

If you have more than two (2) embryos in storage, you must have a FET cycle before starting another fresh stimulated cycle.

Embryos at PIVET are generally frozen on Day 5 or 6 however on request, they may be frozen at Day 3. To be suitable for freezing, embryos must be of high quality, dividing at the expected rate and have only a few fragments. Fragments form as cells degenerate and a high degree of fragmentation is a sign of poor development.

At PIVET your embryos will be frozen using a relatively new technique called **vitrification**. Vitrification is an ultra-rapid form of freezing where embryos go from room temperature at 25 C to - 196 C in less than 1 second. The embryo is instantaneously frozen in a glass like state. Vitrification has shown to increase the survival of embryos over traditional slow freezing techniques at all developmental stages. Survival rates of above 95% for all stages of embryos are common at PIVET.

11. LUTEAL SUPPORT

After your embryo transfer, the embryo will (hopefully) implant and grow. Pregnancy can be identified approximately 12 days later by a simple but specific hormone test referred to as Q β hCG (Human Chorionic Gonadotrophin).

Ovaries sometimes may not produce enough progesterone on their own to support a pregnancy and most stimulation regimens would have limited your ability to produce sufficient hormones to maintain the uterus in a receptive manner. Extra medication such as Pregnyl, Ovidrel, progesterone pessaries or combined(oestadiol and progesterone) pessaries may be prescribed by your doctor until the cycle outcome is known. Your doctor will prescribe a series of medications to either stimulate the aspirated follicles to make hormones (for IVF cycles) or to act on the uterus directly. These luteal phase medications should be continued until you are advised to stop by the nurses (if you are not pregnant) or continued (if you are pregnant).

The waiting time between transfer and the final pregnancy test, usually 14 days post-transfer, can be a difficult time whilst awaiting the result of treatment. Many patients find this period stressful and have difficulty focussing on their daily activities and work routines. Some patients experience mood swings and some of these reactions can be blamed on hormones, but mostly it is the stress of expectation and the difficulty of facing a negative outcome. You may have questions or concerns which can be raised with nursing staff and counsellors who are all available to help you during this time.

12. PREGNANCY TEST

Quantitative β hCG is the hormone we measure in the blood. It is from this level that we determine if you are pregnant.

At PIVET we also measure the level of Oestrogen (E_2) and Progesterone (P_4) in your blood as these hormones are important in maintaining a pregnancy. If they are low, we will offer you medication to increase these levels.

The final blood test must be undertaken even if you have bleeding that is suggestive of a period.

Bleeding in early pregnancy is very common and must be managed appropriately.



Pregnyl / Ovidrel injections raise the β hCG blood level, therefore home pregnancy kits may give a false positive result and we recommend these not be used in fertility treatment cycles. Your period may also be delayed following these injections if the treatment cycle has been unsuccessful.

Even prior to implantation, the early development cells do secrete small amounts of β hCG which may be detected on our very sensitive tests. At PIVET, we require a level greater than 25 IU/L to indicate an implanting embryo (i.e. pregnancy). For this reason we defer the blood test until 16 days after ovulation when the β hCG is usually ≥ 100 IU/L, indicating a pregnancy which is more likely to be ongoing. Levels below 100 IU/L can be seen when the test is undertaken less than 16 days post ovulation, when there has been delayed implantation or if there are low hormonal levels (E_2 and P_4). In the latter case, such pregnancies can still be successful following the addition of support hormones.

In suspect cases, we would repeat the β hCG test after three days, during which time the normal β hCG rise should double.

What happens next?

If the β hCG, E_2 and P_4 results indicate a pregnancy, that is great news and you will need to return weekly for four more weeks to make sure these hormone levels are increasing adequately. Failure of the β hCG to rise adequately usually means an impending pregnancy loss. At the 7th week of pregnancy (i.e. 3 weeks following your positive pregnancy result), you will need to book an appointment for an ultrasound and a review with your Doctor. Please book these appointments by calling PIVET.

Please refer to Section 8 for pregnancy monitoring information

If you have a negative result and wish to do another IVF or frozen embryo transfer cycle, then an ultrasound and a doctor's review appointment will need to be made approximately 3 weeks from the 1st day of your next period. Please call PIVET on 08 9422 5400 to make a "Day 21" appointment. If you do not wish to proceed with any further treatment, you are more than welcome to attend an appointment with your Doctor to discuss the treatment outcome and further discuss your final decision.

Alternatively you may wish to book a counseling session to discuss closure of treatment. Please be aware that nursing staff are available for support and can organise a counseling session if required.

13. OTHER HORMONAL STIMULATION DRUGS

1. Growth Hormone and other Adjuvants for IVF

Approximately 35% of women do not achieve a livebirth from current IVF regimens and many seek adjustments, adjuvants and add-ons attempting to improve their prognosis. There are 10 areas of physiological focus and over 50 adjuncts are described (see Ref:8). However, none have proven benefit according to the highest statistical requirements for evidence-based medicine. The brightest light among them is that for Growth Hormone, which has been the focus of study at PIVET for more than 12 years.

Published Clinical Outcomes of Growth Hormone studies from the PIVET-Curtin University Collaboration:

1. Yovich JL, Stanger JD. Growth Hormone supplementation improves implantation and pregnancy productivity rates for poor-prognosis patients undertaking IVF. *Reprod Biomed Online*; 2010; 21; 37-49.
a. *n=159 women, 232 IVF cycles with GH*
2. Keane KN, Yovich JL, Hamidi A, Hinchliffe PM, Dhaliwal SS. A single centre retrospective analysis of growth hormone supplementation in poor-prognosis IVF patients. *The BMJ Open* 2017; Doi.Org/10.1136/Bmjopen-2017-018107
n=161 women, 220 IVF cycles with GH
3. Keane KN, Hinchliffe PM, Rowlands PK, Borude G, Srinivasan S, Dhaliwal SS, Yovich JL. DHEA supplementation confers no additional benefit to that of growth hormone on pregnancy and live birth rates in IVF patients categorised as poor-prognosis. *Frontiers Endocrinol* 2018 Jan 31;9:14. doi: 10.3389/fendo.2018.00014. *eCollection 2018.*
n=161 women, 161 IVF cycles GH only, 184 cycles GH-DHEA, 42 cycles DHEA only
4. Yovich JL, Ye Y, Keane KN. Growth hormone adjuvant trial for poor responders undergoing IVF. *Eur J Obstet Gynecol Reprod Biol* 2019; 236: 249-251
5. Regan SLP, Knight PG, Yovich JL, Arfuso F, Dharmarajan A. growth hormone during in vitro fertilization in older women modulates the density of receptors in granulosa cells, with improved pregnancy outcomes. *Fertil Steril* 2018; 110(7): 1298-1310. Doi: 10.1016/j.fertnstert.2018.08.018 *n=10 women, 10 IVF cycles*
6. Keane KN, Ye Y, Hinchliffe PM, Regan SLP, Dhaliwal SS, Yovich JL. Live birth outcomes of vitrified embryos generated under growth hormone stimulation are improved for women categorised as poor-prognosis. *Clin Exp Reprod Med* 2019; *in press*
7. Yovich JL, Regan SLP, Zaidi S, Keane KN. The concept of growth hormone deficiency affecting clinical prognosis in IVF. *Front Endocrinol* 2019 Oct 4;10:650. doi: 10.3389/fendo.2019.00650. *eCollection 2019.*
8. Yovich JL, Ye Y, Regan SLP, Keane KN. The evolving concept of poor-prognosis for women undertaking IVF and the notion of growth hormone as an adjuvant; a single centre viewpoint. *Front Endocrinol* 2019. *In press*

The above studies involved 491 women who had a total 849 IVF cycles where GH adjuvant was used. No significant complications occurred to the women or their babies. Two women had mild swelling and joint pains in their hands, ceasing within a few days of stopping the GH injections.

Costs: Currently PIVET prescribes SciGen GH cartridges at \$300 each. The injections provide 1 IU per day (which is a normal physiological dose) for 15 days. Patients should discuss with their gynaecologist regarding regimens of 15 days, 30 days or 45 days (i.e. One, two or three cartridge course.)

PIVET studies have shown benefits for all the regimens applied, with livebirth rates improving x 2.5-fold up to x 7-fold when total productivity is calculated from fresh and frozen embryo transfers. These results underly PIVET's current strategy to perform single embryo transfers (SETs) only and aim to cryopreserve blastocysts for future frozen embryo transfer cycles (FETs).



Other Adjuvants:

2. DHEA

Following reports from eminent IVF academics in the USA, PIVET developed and has trialled DHEA troches. The theory behind the use of DHEA is that many women with infertility have low androgen hormone levels, particularly those age >35 years. Our research shows that the troches are very effective at improving the full androgen hormone profile as published:

Keane KN, Hinchliffe PM, Namdar N, Conceicao JL, Newsholme P, Yovich JL. Novel dehydroepiandrosterone troche supplementation improves the serum androgen profile of women undergoing in vitro fertilization. *Drug Design, Development and Therapy* 2015; 9: 5569-5578.

However, although there is the theoretical likelihood of enhanced egg quality in response to the improved hormone profile, our PIVET studies have not yet shown to have clinical benefit with respect to IVF outcomes. It is possible that some DHEA benefit is being concealed by the more prominent benefit of GH when the two are being used concomitantly. PIVET is prepared to prescribe DHEA to women who understand these limitations on the basis that the troches are relatively inexpensive and no significant side effects have been seen among more than 1000 women who have used the troches.

The usual regimen is to use the DHEA for 2-4 months prior to an IVF cycle, although we would caution women against deferring IVF treatments, as that has proven levels of effectiveness. The cost of DHEA troches is approximately \$65 per month of use.

3. MELATONIN

Melatonin is a hormone-like substance secreted in the body from the pineal gland and is very involved in controlling the circadian (day/night) rhythms of the body. It has therefore found a place in correcting jet-lag and insomnia of shift-workers. Melatonin has also become recognised as a powerful natural anti-oxidant as well as anti-inflammatory and may therefore enhance the implantation process. So far there is insufficient data to prove whether this is actually occurring, but the agent is natural and free from any significant side-effects.

The recommended regimen is 3mg tablets daily for 6-weeks in the lead-up for IVF. This requires a compounding pharmacist who will require a prescription. It costs around \$40 per 30 tablets.

4. PREDNISOLONE

Prednisolone is a chemical that has been shown to have a positive effect on implantation rates and pregnancy at various centres around the world. Prednisolone has an anti-inflammatory activity and is normally used in cases where corticosteroid therapy is indicated, such as skin and respiratory allergies and autoimmune disease.

In the case of infertility treatment, it can be considered where there has been repeated failed treatments or where there has been a history of recurrent pregnancy loss (miscarriage).

PREDNISOLONE MAY WORK IN A NUMBER OF WAYS

- A complex interaction between the embryo and the endometrium involves hormones, growth factors, epithelial cells, stromal cells, leucocytes and extracellular tissue. Prednisolone may have important effects on these components, modulating the early events of the implantation process.

- Natural killer (NK) cells are known to be involved in the implantation process. Women with recurrent miscarriage and those who have had repeated failed IVF attempts may have elevated levels of NK cells in their blood stream and endometrium. Prednisolone can cause a significant reduction in NK cells after administration.
- Prednisolone has also been reported to significantly improve implantation rates in women with positive antinuclear antibodies (ANA). As the embryo transfer process may be stressful to the endometrium, it has been suggested that Prednisolone may reduce this stress by reducing adrenal gland activity.

In certain groups of women, there have been significant improvements in the rate of implantation. In particular, there have been improvements where there has been repeated IVF failure and/or there are positive ANA's.

Prednisolone in combination with low-dose aspirin was shown in a study by Hasegawa et al to have a positive effect on implantation in women with positive ANA's. They reported pregnancy and implantation rates of 14.8% and 6.8%, respectively for women with positive ANA's. When Prednisolone was administered, these rates increased to 40.6% and 20.3%, respectively.

A further study demonstrated significant improvements in pregnancy and implantation rates in women who were positive to ANA, anti-DNA antibody, and/or lupus anticoagulant. Their pregnancy and implantation rates were 10.4% and 3.8%, respectively for women positive to these conditions, rising to 35.3% and 13.2%, respectively after Prednisolone administration.

While there would appear to be positive effects on the rate of pregnancy and implantation, the majority of chemicals, drugs and/or hormones that are administered may have certain adverse side effects. Short-term administration of Prednisolone in low dosage is unlikely to produce harmful side effects. The majority of adverse reactions result from withdrawal of the drug or from prolonged use with high doses.

The most common side effects include:



- **Gastrointestinal** Nausea, vomiting, increased appetite resulting in weight gain, diarrhoea, constipation, gastric irritation, pancreatitis.
- **Cardiovascular** Salt and water retention may result in hypertension, while reduced salt levels may result in arrhythmias and cardiac arrest.
- **Neurological** Headaches, vertigo, insomnia, restlessness, seizures, mood changes, depression and paranoia, epilepsy, glaucoma.
- **Dermatological** Impaired wound healing, increased sweating, bruising, hirsutism, acne and dermatitis.
- **Endocrine** Metabolism of carbohydrates, suppression of growth is taken by children, cushing's syndrome, disordered menstruation, hypoparathyroidism.
- **Biochemical** Glucose metabolism, leading to diabetes.
- **Immunological** Frequent and severe infections.
- **Musculoskeletal** Osteoporosis, muscle weakness.
- Avascular Necrosis of the hip (very rare).
- In severe cases, deaths have been reported.

5. INTRALIPID

What is Intralipid infusion?

Intralipid is a fat emulsion solution that consists of soybean oil, egg yolk phospholipids and glycerin. It may be recommended by your physician as part of your fertility treatment.

Why is Intralipid used to treat infertility?

Research in both animals and humans has shown that Intralipid may enhance implantation and maintenance of pregnancy for patients with recurrent pregnancy loss or recurrent lack of implantation with IVF. Some types of infertility may be caused by a slightly overactive immune system. When this occurs the immune system can attack egg, sperm, embryo and even a developing fetus. This can result in difficulty achieving pregnancy, maintaining the pregnancy or repeated miscarriages.

Natural Killer (NK) cells are regulated by the immune system. In women who have autoimmune issues, the NK cells can react abnormally to an implanting embryo, treating it as an invading cell and signaling for the body to attack it.

Intralipids have been shown to lower the activity of the NK cells component of our immune system. Studies have found that Intralipid can help to regulate the NK cells, allowing the embryo to implant on the uterine wall and grow normally. Research has suggested that women who have experienced recurrent miscarriages or multiple failed IVF cycles, as a result of NK cell activation, may benefit from the use of Intralipid.

How is Intralipid administered?



Intralipid is given as an intravenous infusion. You will be required to have some blood tests performed and sign a **Consent Form** prior to the infusion. As recommended by your PIVET doctor, Intralipid is scheduled 10-14 days prior to embryo transfer, and a second infusion around the day of “trigger” for IVF patients and before embryo transfer for FET patients.

Your PIVET doctor and/or nurses will let you know the recommended schedule for you.

What are the risks of Intralipid infusions?

The risks of an Intralipid infusion are low. This product has been used for over 30 years now and there are very few side effects. Some patients may rarely experience the following: *fever, chills, nausea, vomiting, chest pain, shortness of breath or an allergic type reaction*. These symptoms usually resolve quickly once the infusion is stopped.

You may not have Intralipid if you have liver failure, renal disease, sensitivity (allergy) to soy products or eggs, or any recent severe medical illness.

Personal preparation for infusion

Please wear loose and comfortable light clothing, as a cannula will be inserted into your arm or hand for the infusion.

Cost of the procedure

The cost of the procedure is \$800 per infusion.

Drug interactions

Before taking Melatonin it is important to discuss with your Clinician the possible drug interactions if you are currently taking any of the following medications:



- Anti-depressants
- Antipsychotic medications
- Anti-coagulants - blood thinning medications
- Benzodiazepines
- Blood Pressure medications
- Beta-blockers
- NSAIDS - ibuprofen (Advil)
- Tamoxifen
- Other - caffeine, tobacco, alcohol - reduces concentrations of Melatonin in the body and therefore the effectiveness

6. ELEVIT & MENEVIT

Planning Pregnancy?

Elevit – Benefits when planning to fall pregnant

It can take time to build the higher levels of nutrients your body will need to support you and your growing baby from conception. Even with the best intentions it can be difficult to get these nutrients from food alone. So if you're planning to fall pregnant, you should ideally start preparing your body by taking Elevit.

Elevit contains essential nutrients to help support your baby's healthy development from conception, including the highest level of folic acid of any pregnancy multivitamin* (800mcg per tablet).

Folic acid is clinically proven to reduce the risk of neural tube defects like spina bifida.*1

Elevit also contains nutrients including iron to help prevent iron deficiency and iodine to assist your baby's brain development. Elevit should ideally be taken from at least one month before you start trying for a baby and continued throughout pregnancy and breastfeeding.

Menevit – Specifically formulated to support sperm health

Sperm health can be affected by lifestyle and environmental factors, such as pollution. Menevit is specifically formulated with a unique combination of antioxidants to support sperm health and fertility for couples planning pregnancy. Menevit should ideally be taken from three months before trying for a baby as sperm's production cycle takes around 74 - 78 days.



Scan for Ovulation Calendar

Elevit and Menevit are available only from pharmacies. For more information speak to your Healthcare Practitioner or visit www.elevit.com.au or www.menevit.com.au. For health related concerns speak to your Healthcare Practitioner.

Always read the label. Use only as directed. If you have had a baby with a neural tube defect/spina bifida, seek specific medical advice.
 *When taken from at least a month prior to and during pregnancy.
 ^ As of September 2014. 1. DeRegil LM, et al. Cochrane Database System Rev 2010; (10): CD007950.
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14. CANCELLED CYCLES

A TREATMENT CYCLE MAY BE CANCELLED FOR THE FOLLOWING REASONS

- ★ Low or unusual hormone levels, consistent with poor prognosis for the cycle.
- ★ Premature ovulation - this almost never occurs provided you remember to take your Syneral spray, Lucrin, Cetrotide or Orgalutran injections as instructed.
- ★ Unexpected illness in either partner or other family crisis.

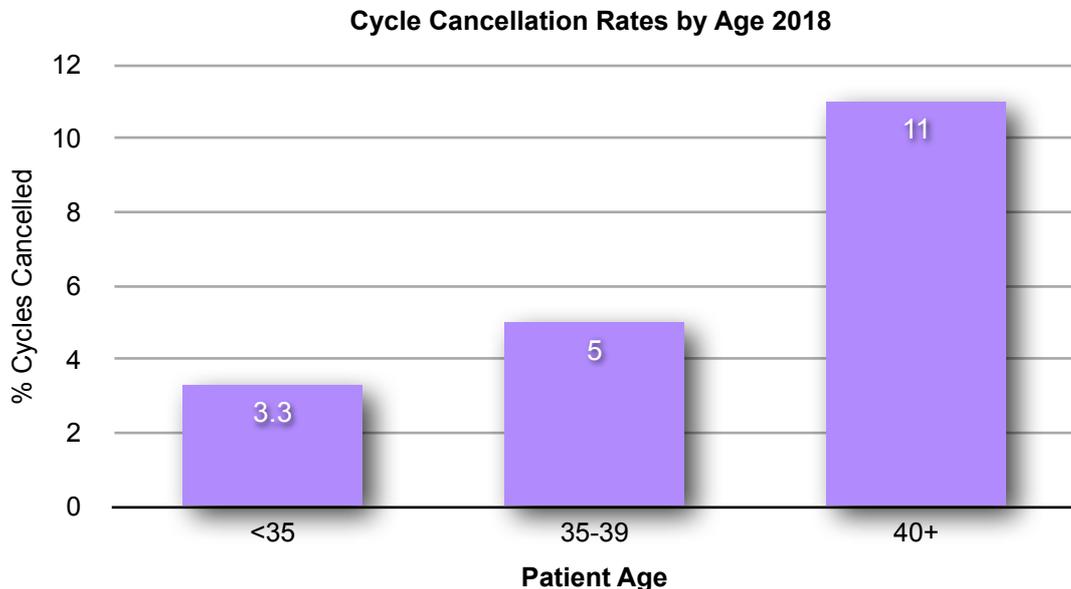
In the event of cancellation, you will be counselled as to the reasons for this. Your doctor will discuss future options for your treatment at your next appointment.

AGE RELATED CYCLE CANCELLATION RATES FOR FRESH STIMULATED CYCLES

In a stimulated IVF treatment cycle, injections of FSH (Follicle Stimulating Hormone) are used to stimulate the ovary to produce follicles and the follicles nurture the developing eggs.

Not all women will respond to the FSH in the same way. Some women produce too many or too few follicles and eggs and treatment may have to be cancelled. If this does occur, do not lose hope as PIVET doctors have a wide range of different drug regimes that can benefit poor or increased responders.

The chance of a cycle cancellation increases with age as the ovary becomes depleted of follicles and eggs.



15. FAILED COLLECTION

This may occur if no eggs are collected at your egg collection procedure. This is now extremely rare, but it can occur especially if we are dealing with low numbers of follicles.

If you do have an unsuccessful collection, you will be allowed to go home and future plans will be discussed with you at the earliest available appointment after this treatment cycle.

16. OVARIAN HYPERSTIMULATION SYNDROME (OHSS)

In order to stimulate the ovaries to produce more than one egg at a time, follicle stimulating hormone (FSH) is used. In general the side effects FSH, if any, are minimal but occasionally include headaches and hot flushes. Between 1 - 2% of women develop a condition known as ovarian hyperstimulation syndrome (OHSS).

Mild manifestations of OHSS are relatively common and include:

- Lower abdominal discomfort
- Abdominal distention
- Mild nausea

Progression of illness is recognised when symptoms persist, worsen, or include ascites (collection of fluid within the abdominal cavity).

Serious illness exists when abdominal pain is accompanied by one or more of the following:

- Vomiting
- Rapid weight gain
- Ascites - accumulation of fluid in the abdomen
- Breathing difficulty, pain on breathing
- Reduced urine output and darker urine

In OHSS the ovaries enlarge and cysts (fluid-filled follicles) develop. The main problem is a profound disturbance of the body's salt and water balance which can have serious consequences. Normally this clears up without much problem, but occasional cases may need hospitalisation and/or intensive care. In **rare** cases, when medical intervention has been delayed, this can have long-term effects including stroke or death.



Risk Factors for OHSS:

- Relative youth
- Underlying hormonal condition known as "polycystic ovarian syndrome"
- Previous OHSS
- If you have greater than 15 eggs collected

The greater the number of follicles produced, the greater the risk of OHSS. Your doctor will discuss the possibility of a "Freeze-all". This is where the eggs will be collected and embryos generated, then all of the embryos are cryopreserved (frozen). In such cases any embryos would be transferred in a later cycle when the OHSS has resolved.

Drinking 2 - 3 liters of fluid including water and isotonic sports drink per day may help the body maintain its salt and fluid balance.

Management:

If anyone **suspects** they are developing any of the symptoms it is essential they should:

- Contact PIVET for early monitoring with the Nursing Staff
- Be available for regular morning follow up visits until condition has resolved

Treatment of OHSS:

This frequently involves no more than rest at home. Occasionally rest and observation in hospital is required with intravenous fluid. In hospital we **may** decide to relieve abdominal pressure with paracentesis (drainage of fluid collecting in the abdomen).

hCG (Pregnyl or Ovidrel) injections may worsen this condition. If you are experiencing any OHSS symptoms and are due to have an hCG injection, withhold your injection until you have contacted a PIVET Nurse or Clinician.

17. FAILED FERTILISATION

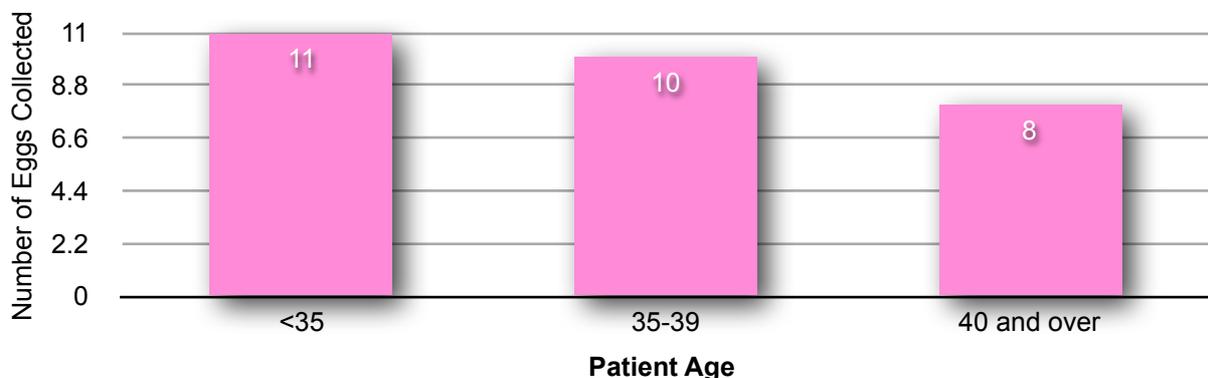
Failed fertilisation is unfortunately a very real possibility with ART treatment. In 2018 the rate of failed fertilisation was 3.1%. It is a very distressing outcome and if it does occur, the possible reasons will be discussed with you by a clinician and embryologist. Failed fertilisation is usually a one off event and is often the result of very low numbers of eggs collected (i.e. 1 or 2 eggs collected). When working with low egg numbers, a failed fertilisation is usually just a probability event. It is however unusual for us to have unsuccessful fertilisation without warning.

If fertilisation fails with standard IVF, you may be counselled on the possibility of using Intracytoplasmic Sperm Injection (ICSI) in a future attempt (*see Fertilisation - IVF and ICSI section*). You are more likely to have a failed fertilisation when standard IVF is used, as the sperm and the egg must communicate perfectly for fertilisation to occur and the sperm must make its way into the egg on its own. This is a very complex process and many things can go wrong. With ICSI, the embryologist does most of the work for the sperm by depositing it inside the egg, therefore there is a reduced chance of fertilisation failure but total failed fertilisation can still occur.

18. AGE RELATED EGG COLLECTIONS

In a typical treatment cycle the average number of eggs collected in 2018 was 10, however this varies from patient to patient. The average number of eggs collected decreases with increasing female age as the number of eggs in the ovary becomes depleted.

Average Number of Eggs Collected by Age in 2018

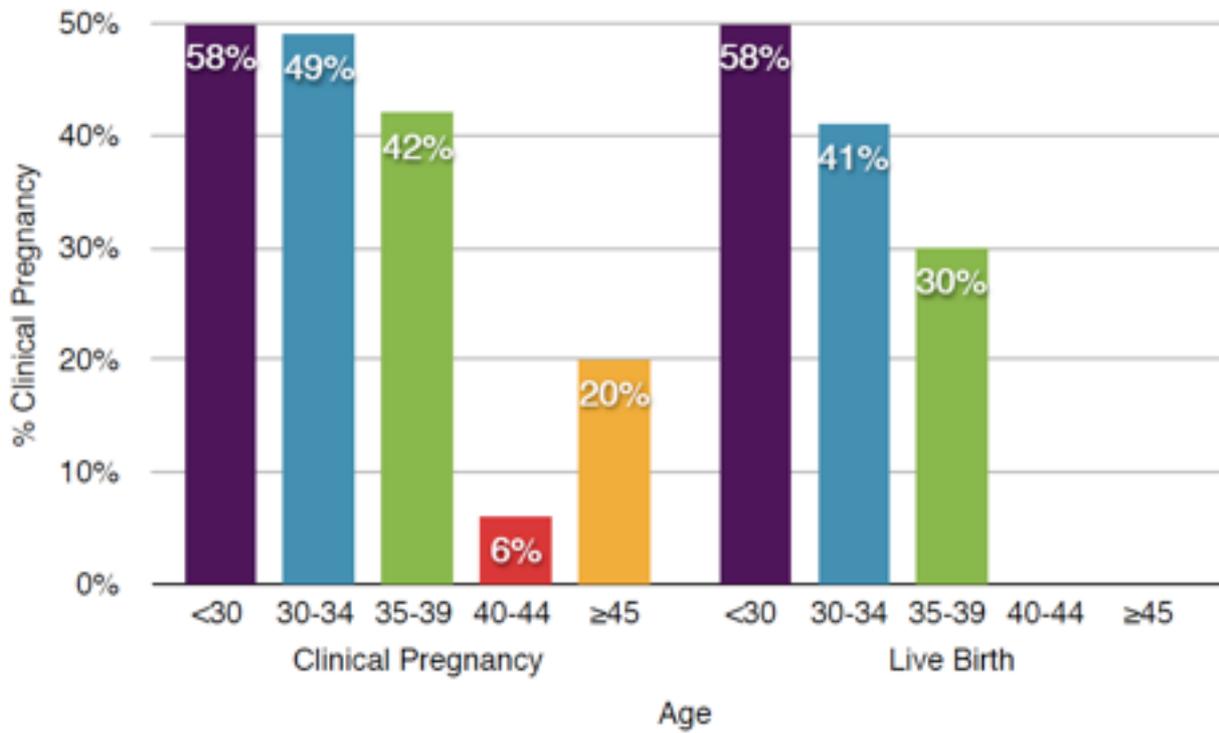


The graph below (*please refer to the next page*) indicates clinical pregnancy rates and live birth rates for 2016. The data above includes both IVF and ICSI treatment, donor embryo and oocyte cycles have been excluded.

- A clinical pregnancy is defined as follows:
 - ➔ The presence of an intrauterine sac (with or without foetal heart) observed on 7 week ultrasound scan;
 - ➔ An ectopic pregnancy;
 - ➔ If a pregnancy is ongoing at 20 weeks.

- A live birth is defined as: *The complete expulsion or extraction from the mother of a baby which shows evidence of life.*

Clinical Pregnancy and Live Birth Rates per Fresh Embryo Transfer Jan-Dec 2018



FROZEN EMBRYO TRANSFER (FET) TREATMENT CYCLE

1. FROZEN EMBRYO TRANSFER

Embryos will be transferred either in a natural cycle (without stimulation), a low dose FSH stimulation cycle or a cycle of Hormone Replacement Therapy (HRT) cycle.

From 2009, most FET cycles are performed using HRT rather than Low Dose Stimulation (see below) to avoid the risks of multiple pregnancy. This decision on which form of stimulation to use will be made in consultation with a clinician.

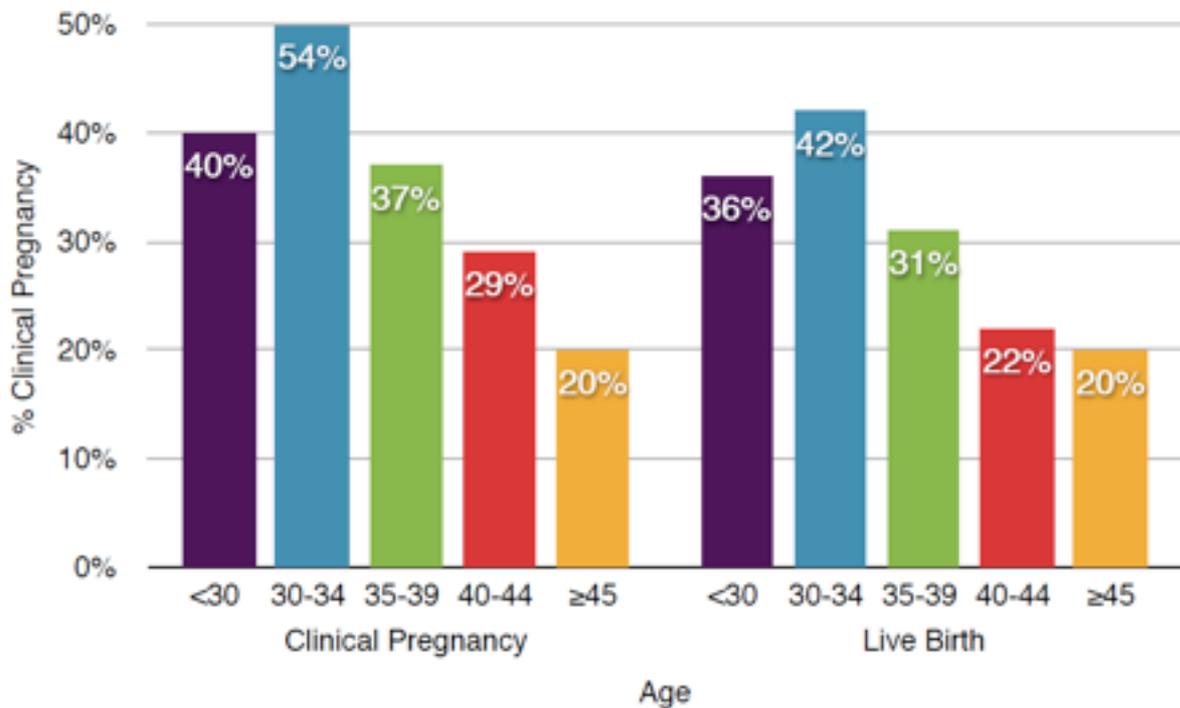
The transfer of the embryos is timed in relation to the age of the embryos and will coincide with the normal ovulation time within your transfer cycle. It is recommended that only one embryo is transferred in your first three treatment cycles (including fresh and frozen) when the oocyte is collected from a women under 40 years of age.

Routinely the embryologist will inform you on the morning of the transfer of the outcome of the thawing process. Sometimes embryos do not survive the thawing process, and if there is any concern that the transfer may not proceed, this will be discussed with you by the embryologist.

A frozen embryo transfer is performed in the same way as for a fresh embryo transfer and a pregnancy test is performed approximately 14 days after transfer.



Clinical Pregnancy and Live Birth Rates per Frozen Embryo Transfer Jan-Dec 2018



2. EMBRYO THAWING

When you request your embryos to be thawed, we return them from - 196 °C to room temperature. Your embryos are passed through a series of solutions to rehydrate them.

The thawing process takes around 10-15 mins. The survival rate of embryos is above 99% and it is rare for an embryo not to survive the thaw.

3. FAILED THAW

Approximately 1 % of embryos do not survive the freeze and thaw process. PIVET uses an ultra rapid freezing technique known as Vitrification. This technique allows for extremely high survival rates when freezing / thawing embryos. If any embryo is severely damaged by the freezing process, it will not be transferred. Embryos will only be selected for transfer if their appearance is good.

Sometimes, although it is rare, embryos do not survive the thawing process and if all your embryos do not survive, the transfer will be cancelled. This is more common with patients who only have 1 or 2 embryos in storage, as there are no backup embryos if they don't survive. If this occurs, an embryologist will speak to you.

Please be aware that the transfer will be **cancelled**, and we will advise that you come to PIVET for a consult with your clinician.



4. NATURAL CYCLES

Occasionally it may be decided that a natural cycle is to be utilised for your FET. Whilst these cycles can be unpredictable, it may be deemed necessary to use this approach due to side effects from a previous HRT cycle. A natural cycle involves hormone monitoring and follicle tracking from Day 2, similar to an IVF cycle. Monitoring occurs to determine when ovulation occurs to enable laboratory staff to time when the embryo transfer should take place.

In some cases, the use of a trigger injection may be used to ensure ovulation does occur and to assist with ensuring luteal hormones provide adequate support during the luteal phase of the treatment cycle.

Therefore it is essential that all patients abstain from intercourse from Day 5 of the cycle until 1 week following embryo transfer to reduce the risk of multiple pregnancy.

5. LOW DOSE STIMULATION CYCLES

As with the natural stimulation cycle, a low dose stimulation cycle may be necessary for preparation of an embryo transfer. This approach uses stimulation of the ovaries with either Tamoxifen tablets or a low dose of FSH (Gonal F or Puregon). The medication is commenced on Day 2 or 3 after performing a baseline blood test. You will then be monitored with blood tests and ultrasounds every second day from Day 9 to assess follicle growth and hormone changes.

During the cycle you will be monitored to assess when ovulation occurs so that the embryo transfer can be timed in appropriately. As with IVF cycles, the use of Tamoxifen, Gonal-F and Puregon is used to stimulate growth of additional follicles in the ovaries. **Therefore it is essential that all patients abstain from**

intercourse from Day 5 of the cycle until 1 week following embryo transfer to reduce the risk of multiple pregnancy.

6. HORMONE REPLACEMENT THERAPY CYCLES

Hormone Replacement Therapy (HRT) consists of utilising Progynova (oestrogen) tablets, oestradiol pessaries, progesterone pessaries and combined pessaries (progesterone and oestradiol) to replace your natural cycle in preparation for embryo transfer. On Day 10 of the cycle, a blood test, ultrasound and an appointment with an embryologist are arranged.

The results of these tests are reviewed and the hormone therapy assessed. Oestradiol pessaries are given for 3-5 days as indicated by blood test and ultrasound results. A blood test may be taken on the 5th day of the oestradiol pessaries to check serum oestrogen levels.

The next stage of HRT consists of progesterone and combination pessaries in conjunction with the Progynova tablets. This therapy will change the quality of the endometrial lining and help in the implantation of the early embryo. The dosages will vary between patients, and the number of days required for these drugs will depend on the age of the embryo to be transferred. It is quite common for the pessaries to cause a discharge from the vagina.

Please discuss any concerns you have with the Nursing staff. On the day of your transfer it is advised that you insert your pessaries rectally rather than vaginally to reduce the chance of having excess residue at the cervix at time of your embryo transfer.

Therefore it is essential that all patients abstain from intercourse from Day 5 of the cycle until 1 week following embryo transfer to reduce the risk of multiple pregnancy.



ADDITIONAL LABORATORY PROCEDURES AND INFORMATION

1. EGG FREEZING

Eggs can now be frozen successfully at PIVET. With the advent of vitrification (ultra-rapid freezing techniques) eggs are able to survive freezing 80-85% of the time.

EGG FREEZING MAY BE USED IN THE FOLLOWING CIRCUMSTANCES



- To preserve your fertility while you are still at a young age giving you time to decide when to start a family (otherwise known as 'social' egg freezing).
- Couples who are not comfortable in producing large number of embryos (i.e. religious reasons) can instead have a specified number of eggs inseminated and the rest frozen for future use.
- If for some reason there is no sperm for insemination on the day of egg collection, eggs can be frozen.
- Patients who require chemotherapy or radiotherapy for illness and are at risk of becoming sterile can also have eggs cryopreserved, as long as drug stimulation is approved by your

specialist.

- Eggs may be stored if there is a risk of premature menopause.

ICSI is required for fertilisation

The first potential concern is that the oocytes may not fertilise at the same rate as freshly collected oocytes because the *zona pellucida*, a cellular coating surrounding and supporting the egg, may be less able to allow sperm to penetrate it and achieve fertilisation following egg freezing and thawing.

This is not a significant problem, since ICSI (intracytoplasmic sperm injection) has been used successfully to achieve fertilisation in thawed oocytes. Whilst ICSI has been used for more than 10 years for the treatment of male infertility, its use to achieve fertilisation with frozen oocytes is relatively new.

The outcomes from ICSI and offspring born through the technique suggest that the ICSI technique itself, has relatively little additional risk.

Chromosome Stability

The second concern involves the genetic viability of the oocytes after thawing. The chromosomes of the mature oocyte collected by routine IVF are contained in a special fine network of fibres called a spindle. The fibres are temperature sensitive and dissolve during the freezing process.

Early concerns suggested that the chromosomes may become unstable after thawing because the spindle fibres may not reform correctly. Recent real time studies have provided significant reassurance that after sufficient time in culture after thawing, the spindles will reform in the majority of oocytes.

Therefore using new protocols and enhanced cryoprotectants, oocyte recovery rates, fertilisation rates, and pregnancy rates appear similar to routine IVF levels such that PIVET Medical Centre believes the technology can be applied clinically with little risk.

Oocyte Selection

The third concern centres on oocyte thaw and utilisation. Current IVF procedures involve the insemination of all oocytes, and the careful selection of embryos created from fertilisation. Oocytes at collection appear very similar and the power for selection at this point is very weak. If oocytes are frozen before insemination and are thawed in a manner to minimise their use or to reduce surplus embryos, then multiple thaw cycles may be required to achieve a pregnancy.

Survival and Fertilisation

Around 85% of all eggs (ova) collected are mature and suitable for freezing. At PIVET only mature oocytes are frozen. This proportion however does vary. There is a risk that some oocytes may not survive thawing and that some oocytes once thawed will remain unfertilised even after ICSI. The reported average survival rate over many recent publications is that 69% of oocytes will remain intact after thawing. The initial results from the developmental work at PIVET is that we anticipate our survival is around 80-85%.

Globally, 63% of all injected eggs will develop signs of fertilisation. This rate is similar to that observed when fresh oocytes are injected. In other words, once the oocyte has survived thawing, its chance of fertilisation and development is the same as for routine IVF. Taking the two risks together, about half of all oocytes frozen will be fertilised. You need to understand therefore that the number of potential embryos is related to the number of oocytes initially frozen. Please be aware that there is a risk that none of the oocytes may survive thawing or all may fail to fertilise.

Ovarian Stimulation and Oocyte collection

The process for stimulating and collecting eggs for freezing is the same as for IVF (see IVF section). Following an egg collection, the eggs are vitrified without insemination with sperm.

How many Collection Cycles will I require?

Some patients have raised the question of the number of oocytes that need to be frozen. This is a difficult question to answer since it is not known how many oocytes will be needed to achieve a pregnancy. In many cases the number of oocytes needed maybe more than can be recovered in single cycle. Therefore depending on why you are considering oocyte freezing, more than one IVF collection cycle may be necessary. Early data from the use of frozen/thawed oocytes suggest they produce blastocysts (Day 5/6 embryos) at about half the rate of fresh eggs (so around a 20% blastocyst rate) therefore it is advisable to maximise the number of eggs you have frozen.

Legal limitations on Storage and Use of Frozen Oocytes



While there are no laws within the **Human Reproductive Technology Act** governing the freezing of oocytes, there are laws that govern their storage and use. The HRT Act has prescribed that the maximum period of storage of gametes (either eggs or sperm) is **15 years** after which they **must** be discarded. Continued storage will require a specific approval for an extension from the **Reproductive Technology Council**.

VERY IMPORTANT INFORMATION BELOW

There are also laws that restrict the creation of embryos in WA to infertile couples only. One may anticipate that if you need to use the frozen oocytes in the future, then you have been unsuccessful in your normal means at conception. However, if you are not infertile, then HRT Act laws prohibit IVF without approval and Medicare support may not be available.

Oocyte (egg) Freezing

If oocyte freezing is considered part of your treatment management, then part of the cost of IVF (hormone medication, pathology and ultrasound test, medical treatment, etc) will be covered by Medicare. There will be only a small additional charge for freezing of the oocytes.

Social Oocyte Freezing

Social oocyte freezing (i.e. preserving your fertility) is not covered by any Medicare rebate. You will need to contact PIVET Administration for an estimate of the cost for oocyte collection and freezing.

Depending on the age at which the cycle is undertaken or your fertility parameters (AMH/AFC), there may not be an abundance of oocytes to preserve, so please be realistic with your expectations given the high cost of this procedure.

Please be aware there is **no guarantee** the cycle will: *proceed to collection, or oocytes will be collected, or oocytes will be mature enough to be frozen, or they will survive when warmed, or they will fertilise and produce embryos that are suitable for transfer.* Early data from the use of frozen/thawed oocytes suggest they produce blastocysts (Day 5/6 embryos) at about half the rate of fresh eggs (so around a 20% blastocyst rate) therefore it is advisable to maximise the number of eggs you have frozen.



Please discuss the possibility of these outcomes with your doctor before committing to treatment.

There will be also be an ongoing annual fee for oocyte storage.

2. LONG TERM EMBRYO STORAGE



Long-term storage of frozen embryos is not recommended. In Western Australia, State Legislation governs practices concerning ART. The Human Reproductive Technology Act of 1991 stipulates a maximum embryo storage period of 10 years.

To extend storage beyond 10 years, you must apply to the Reproductive Technology Council (RTC) and be granted an approval. A reminder will be sent to you at after 9 years and 9 ¾ years to prompt you that storage expiry is approaching.

We will attempt to contact you 3 months before the expiry date to ensure that you have come to a decision on your embryos.

If you wish to extend the storage period, an application will have to be made to the RTC and depending on the reason for continued storage, an extension may be granted. Such an application must be received by the RTC **1 months prior** to the expiry of the 10 year limit.

If no application is received by the RTC or approval to continue storage is not given, legally PIVET will have to allow your embryos to succumb on the day the storage limit expires.

It is your responsibility to keep PIVET advised of your contact details so that we can forward the documentation for you to complete and send to the RTC.

Legislation prevents PIVET from offering ART (Assisted Reproductive Technology) to patients presenting with symptoms of menopause

PIVET may ask that you have a medical review of your menopausal status if you are over 45 years of age prior to renewal of your embryo storage.

If you are not eligible to have embryos transferred because of menopause or poor health, PIVET will ask that you consider donation to their *Embryology Training Program* or donation to another couple or remove the embryos from cryostorage.

3. MICROSURGICAL EPIDIDYMAL SPERM ASPIRATION (MESA)

Also referred to as a MESA (*Microsurgical Epididymal Sperm Aspiration*), the procedure is performed under a general anaesthetic to obtain sperm from a man who has previously had vasectomy, or to further investigate and retrieve sperm from men who have extremely low numbers of sperm or azoospermia (no sperm in the semen).

During the first consultation at PIVET, various laboratory and clinical tests are recommended for both partners in order to find out the possible causes of infertility. Semen analysis is one of the laboratory tests carried out to assess the male partner. This test will estimate whether sperm cells are present or not in the ejaculate. If there are no sperm cells present, a repeat test may be organised to confirm the findings. The Clinician will review the findings and arrange medical treatment accordingly. The condition described above where no sperm cells are found in the ejaculate is called azoospermia.



Azoospermia results due to a blockage or missing tubes which carry sperm from the testes (where sperm is produced) to the exterior, or due to absent sperm production in the testes. It is sometimes possible to collect sperm from the male genital tract, especially the testes and the tube close to the testes called the epididymis. This surgical procedure requires general anaesthesia and takes approximately 30 - 45 minutes to perform. Sperm collection is usually carried out at the preliminary clinical investigation stage.

During the MESA, a small tube is introduced into the epididymis and milky fluid containing the sperm is aspirated. The aspirate is emptied into culture medium, counted and frozen (cryopreserved) for future infertility treatment.

MESA sperm are prepared using the standard IVF methods to isolate the best quality sperm for ICSI of eggs recovered from the female. Surplus sperm remaining following the ICSI treatment is usually cryopreserved. The cryopreserved sperm can be used for future ICSI attempts and this will prevent the male partner from having to go through another MESA procedure. For cryopreservation, the sperm suspension in the culture medium is mixed with an equal volume of the cryoprotectant solution, loaded in to plastic straws and cooled gradually. Finally the sperm straws are placed in liquid nitrogen for storage. Cryopreserved sperm are also prepared in a similar way to fresh sperm during the future treatment attempts. The procedure is performed in the morning, takes approximately an hour and most patients can go home at around 3pm.

Risks and complications are rare, but may include:

- Infection
- Moderate to severe discomfort Bruising
- Swelling
- Redness
- Testicular scarring
- Impaired testicular function
- Heavier than usual blood loss
- Anaesthetic complications



4. TESTICULAR BIOPSY & TESTICULAR SPERM ASPIRATION

In conditions where sperm production is extremely low, so low that no sperm can be found in the semen or the epididymis, it is sometimes necessary to look for sperm in the testis itself through a procedure called testicular biopsy. A testicular biopsy may be needed in situations where there is a congenital loss of reproductive ducts or as a result of scarring and blocking of the fine tubules that lead from the testis as a result of infection or damage to the testicles.

A biopsy of the testis is performed under general anaesthetic in PDSC and in 50% of cases, adequate sperm numbers can be obtained by carefully processing the biopsy tissue to find small "islands" of sperm production that persist despite damage elsewhere in the testis. Sperm taken from the testes, often show very little movement and therefore can only be used to fertilise an egg if they are injected into the egg using ICSI. The results of the ICSI procedure with testicular sperm is a 39% clinical pregnancy rate from one egg collection cycle.

Testicular Sperm Aspiration

In some situations a fine needle biopsy of the testis can be performed. This is usually only performed if a patient is having trouble producing a sample on the day of collection or if a patient is unable to have a MESA or testicular biopsy.

This involves local anaesthetic placed into the testis which makes it numb. A fine needle is then placed into the testis and a small piece of tissue is removed or sperm can be taken from the epididymis itself. An embryologist then examines the fine tubules contained in the biopsy sample and removes sperm from these tubules for use with ICSI. The fine needle biopsy takes about 15 mins. Any leftover sperm may be frozen or the biopsy procedure can be performed again on subsequent cycles if needed.

5. SPERM FREEZING

It is possible to freeze and store sperm for use at a later date. This technique has been used successfully since the 1950's. It involves the mixing of your samples with a cryoprotectant (a freezing liquid) and drawing the sample into several specific, labelled straws. After freezing, samples are stored in liquid nitrogen tanks.

It is useful to freeze sperm in a number of instances, including:

- Prior to having a vasectomy.
- Prior to surgery.
- Pre-chemotherapy treatment, and also prior to exposure to any toxins that may possibly have adverse effects on sperm quality or production.
- If the male partner is likely to be unavailable to produce a semen sample at the time of his partner's treatment.
- In cases of impotency.
- Where the semen quality is variable between one sample and the next.
- In cases of sperm retrieval from the testis or epididymis.

There are several key pieces of information you need to be aware before you sign a request to freeze your sperm.

These are as follows:

- You will need to sign a consent form before we can freeze any of your samples.
- You will also need to have several blood tests before freezing. Since your samples are stored with many other samples in large insulated tanks filled with liquid nitrogen (dewars), it is important that we know that you do not pose any infection risk to the other samples. If you do not test positive to HIV, Hepatitis B and/or C and Syphilis, we believe there is a very low risk of contamination from storing your samples with others that have also returned a negative test.
- If for time or logistical reasons, you do not have a completed blood test before freezing, then your samples can be stored but in a tank with other samples that have also not been tested. The infection risk is most likely low but cannot be known.
- As it is known that some virus and bacteria can survive in liquid nitrogen, if you do test positive for one of these tests, we can still store your samples in special quarantine dewars.
- The samples are stored in a number of securely labeled special cryogenic straws in liquid nitrogen labeled with key identifying information. The number of straws will vary between samples. As a general rule one sample may only be suitable for 1-2 cycles of treatment and that more than one sample may be recommended. Usually one straw is suitable when used in conjunction with IVF/ICSI.
- That not all sperm will survive freezing and some samples may be of sufficient poor quality that Advanced Reproductive Techniques (IVF/ICSI) may be required should the samples be required to achieve a pregnancy.
- There have been a large number of children born from frozen sperm / semen to provide confidence that there is no substantial risk from the process. Even so, there can be no guarantee that pregnancy will ensure.



As per the *Human Reproductive Technology Act 1991, Directions 6.8*, sperm samples may be stored for a maximum period of 15 years. A reminder will be sent to you after 14 years and 14 ³/₄ years to prompt you

that storage expiry is approaching. To extend storage beyond 15 years, you must apply to the Reproductive Technology Council (RTC) and be granted an approval.

PIVET will send you the application to extend storage. Such an application must be received by the RTC **1 months prior** to the expiry of the 15 year limit. If no application is received by the RTC or approval to continue storage is not given legally PIVET will have to allow your sperm to succumb on the day the storage limit expires.

It is your responsibility to keep PIVET advised of your contact details so that we can forward the documentation for you to complete and send to the RTC.

One major concern is that you will move address and lose contact with PIVET, such that your “annual request” for continued storage will lapse. Please note that if you fail to maintain contact with PIVET, your samples will be discarded after the return of three (3) consecutive letters of notification.

6. ASSISTED HATCHING

The outer shell of the embryo (called the zona pellucida or “zona”) can sometimes become hardened or thickened, resulting in the embryo having difficulty “breaking” out of this shell to attach to the uterine wall. It is possible to make an opening in the zona pellucida to help the embryo escape from shell, and this is called Assisted Hatching.

It is performed a number of ways, by either cutting a slit in the zona using a fine glass needle, by drilling a hole in the zona using acidic culture medium or by using a laser to open a hole in the zona. At PIVET a laser is used for assisted hatching.



It is hoped that this technique will improve the chance of your embryos implanting in the uterus and resulting in a baby. Dr Jacques Cohen and his team are the pioneers of assisted hatching. They trialed this technique in their IVF program in an unselected group of patients and they found that the multiple pregnancy rate increased to 42%. This was mainly because of improved implantation rate of embryos transferred and also due to the possibility of embryos splitting in two as they pass through the opening made in the zona.

At present, the number of babies born through the application of assisted hatching is small. Therefore the results obtained will be analysed regularly to assess the safety of this technique.

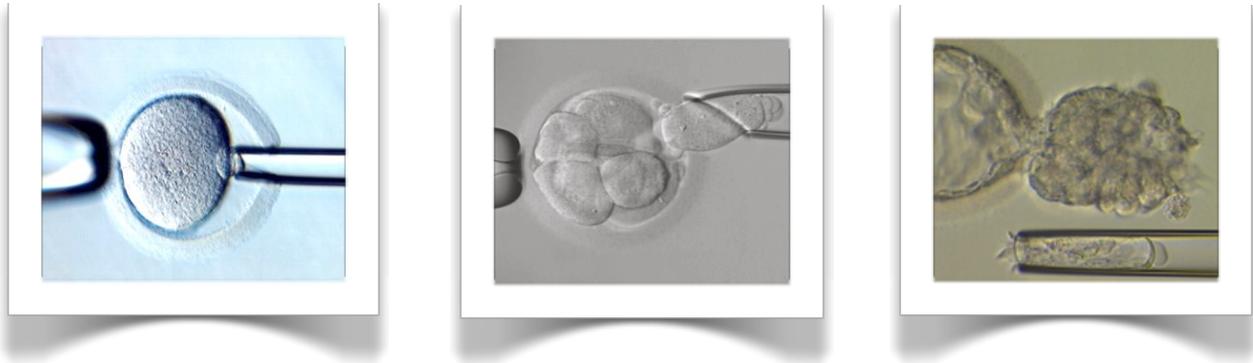
7. EMBRYO GLUE / VITROLIFE MEDIA

Embryo Glue is a culture media that is used to transfer embryos back into the uterus. It differs from our standard culture media in that it contains a compound called Hyaluronan, a complex macromolecule found in the tubal and uterine fluid of many species. Data suggests that it is involved in fertilization, embryo development and implantation and that its activity peaks around embryo implantation on Day 5. Some EmbryoGlue is transferred with the embryo(s) back into your uterus.

EmbryoGlue is an extension of the our culture media but with increased amount of Hyaluronan. It has been proposed that EmbryoGlue may be beneficial at transfer by allowing improved mixing of the embryo with uterine secretions and that is could act as a binding agent between uterine lining and the embryo. There are some reports of higher pregnancy rates especially after the transfer of frozen embryos however, other unpublished presentations have not supported these observations. There is no data to suggest that using EmbryoGlue is detrimental to embryos.

EmbryoGlue is available to PIVET patients. There is a charge for using it that can be discussed with the accounts department. If you are interested, please speak to your Clinician.

8. PRE-IMPLANTATION GENETIC SCREENING (PGS) OR ANEUPLOIDY SCREENING



Above: L - R: Biopsy of oocyte (egg), blastomere (3-day-old embryo) & trophectoderm biopsy of a 5-day-old embryo

It is estimated that a high percentage of embryos are affected by genetic abnormalities not apparent in the parents, but thought to be caused by chromosomal problems that arise spontaneously in the egg, sperm or embryo.

The process that results in embryos having extra or missing chromosomes is an unpredictable or unpreventable accident of nature. These changes to the chromosomes may lead to implantation failure, recurring miscarriages or the development of children with disorders such as Down's Syndrome. Aneuploidy refers to the occurrence of one or more extra or missing chromosomes.

Some categories of people are known to be at greater risk of these problems than the general population. Aneuploidy screening is approved for the following categories of people who are eligible for the IVF program and who are considered to be at significant risk of producing an embryo that is chromosomally abnormal:

- Women over 35 years of age providing eggs.
- Women with ≥ 2 miscarriages.
- Women with ≥ 2 failed IVF attempts where embryos have been transferred.
- Women referred by a clinical geneticist with a family history of aneuploidy not caused by translocations or other chromosomal rearrangements.

PGS now provides these higher risk patients with the option of screening embryos for chromosomal abnormalities before implantation of the embryos.

Prior to recent changes to the law in Western Australia, the only options available under these circumstances were to use pre-natal diagnosis (either amniocentesis or chorionic villi sampling), with the possibility of termination of the pregnancy if the results of these tests were abnormal, or to consider the use of donor gametes.

At PIVET, with the assistance of Monash IVF (Melbourne) or Natera (California, USA), PGS will involve the following steps:

- Fertilisation by ICSI
- Zona hatching
- Blastocyst culture
- Embryo biopsy
- NGS (performed at Monash IVF, Melbourne) or SNP-array (performed at Natera-California, USA)

IVF / ICSI - Why do we use this procedure?

This allows a number of oocytes to be collected and fertilised using microinjection of a single sperm into each oocyte. This reduces DNA contamination by other sperm that may be present following conventional IVF. Following fertilisation the embryos are cultured in the laboratory for a further 4/5 days. Embryo biopsy is then performed on Day 5/6 embryos.

Zona Hatching and Embryo Biopsy

The process involves creating a hole in the zona using an infra-red Laser. This is the same technique as Assisted Hatching employed by PIVET for several years. 5 - 10 cells from the trophectoderm of the blastocyst (the part of the embryo that forms the placenta) are then removed from the embryo using a very fine glass pipette.

CGH and blastocyst culture

The biopsied cells are then transferred to tubes, frozen and either shipped to Monash IVF in Melbourne or Natera in California, USA. During this time, the biopsied embryos are frozen until the results are obtained which may take 2-3 weeks. Once the results are obtained, and if there are any normal embryos for transfer these can be transferred in a frozen embryo transfer cycle.

There is no guarantee that following the above tests that the baby will have normal chromosomes. While embryo biopsy is used widely throughout the world and does not appear to have adverse affect on the embryo's potential to implant, obtaining a result from every embryo may not be possible.

There are several reasons for this including:

- Some embryos may not be of sufficient quality to biopsy.
- Test results may not be conclusive in some embryo.
- A proportion of all embryos made are not genetically healthy.
- Not all cells in an embryo are genetically identical.

Aneuploidy screening is performed on all 23 chromosomes plus the sex chromosomes (X and Y). Screening for these chromosomes can detect chromosomal errors that result in miscarriage, and chromosomal abnormalities that have the potential to go to term. Technical limitations in the CGH test indicate an error rate of approximately <1%. There is not an absolute guarantee of normal chromosomes on the embryo as a result of analysis, as this may not be representative of the whole embryo.

Since some biopsied cells may produce inconclusive results in the testing process and some embryos are not genetically healthy, few embryos tested may be available for transfer or freezing. Moreover, in some cases, there are no embryos of appropriate quality to transfer. If you request aneuploidy testing and there are insufficient embryos to make PGS a viable option, you will be counseled about adjusting your treatment program.



9. PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

What is Preimplantation Genetic Diagnosis (PGD)?

PGD is a technique used to screen IVF embryos for a specific genetic condition (*Single Gene Disorders*) or chromosome rearrangement (*Translocations*).

Couples who are at risk of transferring a genetic condition to their children or who exhibit a translocation can undergo this procedure.

What are Single Gene Disorders?

Single Gene Disorders are genetically inherited disorders. Patients with a history of these disorders who are at risk of passing their disorder onto their children, can utilise PGD.

This test will aim to distinguish between embryos without the disorder, those that are carriers of the gene but not affected and those that are affected by the disorder. There are many disorders that can be tested using PGD. Some are Cystic Fibrosis, Thalassaemia, Huntington's disease and Fragile X.

What is a Translocation?

A translocation is a rearrangement of chromosome segments between two different chromosomes. There are two types of translocations, Robertsonian and reciprocal.

Robertsonian results when a whole arm of a chromosome is exchanged, while reciprocal involves a part of chromosome swapping with another part of a different chromosome.

Carriers of these translocations are at risk of producing sperm or eggs with an "unbalanced" form of their translocation (i.e. not all the genetic material is exchanged). When these form an embryo, this can result in failure to implant, miscarry or the birth of a chromosomally abnormal child.



At PIVET with the assistance of Monash IVF, Melbourne - PGD will involve the following steps:

- Feasibility testing.
- Fertilisation by ICSI.
- Zona hatching.
- Embryo biopsy.
- Blastocyst culture.
- PCR (Polymerase Chain Reaction) or NGS (performed at Monash IVF, Melbourne) or SNP-array (performed at Natera California, USA).

Feasibility Test

A Feasibility Test is carried out on patients with a previously identified translocation or single gene disorder. The test is to confirm that the disorder or translocation in question is present and to determine the optimal test conditions for either NGS, SNP-array or PCR. The testing is done on blood samples collected from both partners and any children born. The samples are then sent to Monash IVF, Melbourne or Natera California, USA for testing.

Fertilisation, Zona Hatching and Embryo Biopsy - See "PGS and Aneuploidy" above.

Testing and Blastocyst Culture

The biopsied cells are then transferred to tubes, frozen and either shipped to Monash IVF in Melbourne or

Natera in California, USA. During this time, the biopsied embryos are frozen until the results are obtained which may take 2-3 weeks. Once the results are obtained, and if there are any normal embryos for transfer these can be transferred in a frozen embryo transfer cycle.

There is no guarantee that following the above tests that the baby will not have the single gene disorder or have normally arranged chromosomes. While embryo biopsy is used widely throughout the world and does not appear to have adverse affect on the embryo's potential to implant, obtaining a result from every embryo may not be possible.

There are several reasons for this including:

- Some embryos may not be of sufficient quality to biopsy.
- Test results may not be conclusive in some embryo.
- A proportion of all embryos made are not genetically healthy.
- Not all cells in an embryo are genetically identical.

Since some biopsied cells may produce inconclusive results in the testing process and some embryos are not genetically healthy, few embryos tested may be available for transfer or freezing. Moreover, in some cases, there are no embryos of appropriate quality to transfer.

If you request aneuploidy testing and there are insufficient embryos to make PGS a viable option, you will be counselled about adjusting your treatment program.

PERTH DAY SURGERY CENTRE

1. ABOUT PDSC



PDSC was granted a license in 2006 by the Health Department of Western Australia as a provider of gynaecological, andrological and urological services for the management of fertility.

The day surgery is one of a kind in that it is located at PIVET Medical Centre offering a comprehensive assisted reproductive technology service, ensuring optimal convenience for clients.

The PIVET Medical Centre - Perth Day Surgery Centre “all-in-one” approach in the management of fertility is accommodated by the utilisation of an expert team that includes scientific and technical personnel.

Please Note: Our PIVET Clinicians operates under a “team approach” and are rostered for set procedure lists in our day hospital, Perth Day Surgery Centre.

Dependent on your allocated procedure day in our day hospital, you may be treated by a different Clinician from our team of Fertility Specialists.

You can see your preferred Clinician for PIVET clinic consults - please request this from our friendly reception staff.

2. ACCREDITATION AND REGULATION BODIES

Perth Day Surgery Centre is accredited with:

- ★ Licensing and Accreditation Regulatory Unit, Department of Health, Western Australia.
- ★ NSQHS Standards
- ★ AS/NZS ISO 9001:2015

For more information, please visit our website: www.pivet.com.au.

3. COSTS

Our centre has a schedule of fees for procedures in the day surgery. Depending on your type and level of private insurance, these fees may vary so we encourage you to check with your insurance provider regarding your excess and rebates.

There will also be additional costs when your procedure requires the administration of an anaesthetic by an Anaesthetist. The Anaesthetist on duty will discuss this with you on the day of your procedure. Please contact our administration staff for further information on 08 9422 5400.



4. DAY SURGERY

Day surgery refers to the admission and discharge of a patient on the same day as their procedure. This setting is ideal for patients requiring minor and IVF related procedures.

Our day surgery was custom built with this in mind, and a typical day for us starts at 0830 am with egg collection procedures, followed by other procedures requiring an anaesthetic, then procedures that do not require sedation such as embryo transfers.

You will receive a scheduled time for your procedure, and we will need you to arrive at the day surgery either 1 hour or 30 minutes prior to this time depending on your anaesthetic requirements:

- On admission, patients are interviewed by various members of our team, your blood pressure and pulse may also be recorded at this time.
- You will be asked to change into a gown, and then escorted by a nurse into theatre where your procedure will take place.
- After your procedure is completed, you will be taken through to recovery where you will be closely monitored.
- If you require an anaesthetic, you can expect to be with us from admission through to discharge for approximately 3 - 3.5 hours, however individual circumstances may alter this time.
- We welcome your partner, or support person, to accompany you to the day surgery. If your procedure does not require administration of anaesthesia by an Anaesthetist, your partner / support person can be with you in theatre should you wish.
- If you are having anaesthesia, you are unable to drive a motor vehicle for 24 hours after discharge. Also, please arrange to have someone you know transport you home, and be with you for 24 hours following discharge. If these requirements cannot be met, we may not be able to proceed with your procedure.

5. WHAT TO BRING

- Any admission paperwork you have.
- Your private fund details.
- Medicare card.
- Credit card or cheque book.
- Reading material.
- Your treatment schedule (if you have been given it prior by the clinic nurses).
- Comfortable clothes for when you go home.
- Your support person.



6. FRAGRANCES

For the health of our eggs, sperm and embryos we do ask that you, and those accompanying you into the day surgery, do not wear perfumes, aftershaves, colognes, heavily fragranced make up or other heavily scented personal hygiene products.

We also advise you, and those accompanying you into the day surgery suite, to not smoke prior to your procedure (*and preferably after too!*).

7. DELAYS

We appreciate that your time is precious, so if you find you're waiting longer than anticipated for your procedure, we will do our best to ensure any delays are kept to a minimum. Alternatively we can make other suitable arrangements for you.

8. DISCHARGE

When you are ready to go home from the day surgery, our nurses will check that you have:

- Someone you know escorting you home.
- Someone who can help care for you in the hours following your procedure (where applicable).
- Your post-procedure information sheets.
- Your medication / treatment schedule, plus any prescriptions you may require
- Any questions answered.

It's always a good idea to have your partner or support person present while our nurses are going through your discharge instructions because it's easy for you to forget things after you've had an anaesthetic.



9. ANAESTHESIA

If your procedure requires the administration of an anaesthetic, our theatre staff will book you an admission and procedure time. You will also receive a pre-procedure confirmation call in the days leading up to your procedure to discuss arrangements for admission and discharge.

We will generally ask that you arrive for admission 1 hour prior to your scheduled procedure. This allows us time to admit you and administer any pre-operative medications that may have been ordered. Our Anaesthetist will see you on the day of your procedure during your admission, and some will telephone you 1 - 2 days before your procedure.

For certain procedures it is necessary to administer a general anaesthetic, however for most procedures, a light (twilight /neurolept) anaesthetic is more appropriate. This light level of anaesthesia also allows you to wake up very soon after the procedure is completed and it's this type of anaesthetic that is preferred for egg collections and HyCoSy's.

It is a good idea to find out if anyone in your family has ever had any problems associated with anaesthesia, or previous operations. Also mention to theatre staff, as well as the Anaesthetist, what past procedures you've had, and if you experienced any problems or complications.



10. FREQUENTLY ASKED QUESTIONS - FERTILITY TREATMENTS FOLLOWING "DAY PROCEDURES"

Q: Can I continue exercising following my egg collection, embryo transfer or intra-uterine insemination?

A: Following your procedure and until your pregnancy test, we ask that you avoid any strenuous exercise where you become short of breath.

Strenuous exercising elevates your core body temperature, and following egg collection, could lead to increased swelling, torsion or heavy bleeding of the ovaries. Likewise do not use saunas or have very hot baths. Also try to avoid heavy lifting.

Q: I've had my embryo transfer / Intrauterine insemination what should I be doing?

- Light exercise / light duties only.
- It is advisable to avoid alcohol and smoking during the time also.
- Drink 6 - 8 glasses of water a day.
- Take a supplement containing Folic Acid.
- Avoid herbal / Chinese medicines.
- Check with your doctor or pharmacist before starting other medications.
- Avoid very hot baths / saunas.
- Eat a well balanced diet.
- Abstain from sexual intercourse for 7 days following your embryo transfer.



Q: Can I receive acupuncture during my treatments?

A: Yes, you may have acupuncture during your treatment cycle, and following your embryo transfer.

Q: What can I take if I have a headache, or any aches or pains?

A: Paracetamol medications such as Panadol, Panamax and Panadeine are safe to take should you need it. It is not recommended to take more than 8 tablets within 24 hours. If these medications are not providing relief, please contact the clinic (or after-hours doctor) for further advise.

There is some thought (although unproven) that non-steroidal anti-inflammatory (NSAIDs) pain killers (e.g. Nurofen, Naprogesic, Ibuprofen etc.) may interfere with the process of embryo implantation, so it is advisable to avoid these following your egg collection and embryo transfer.



Q: Is it normal to have cramps after the egg collection, intra-uterine insemination, or embryo transfer?

A: All of the hormones that your body has produced in response to your medications can make your ovaries larger than what they normally are, as well as more active than usual.

Therefore, you may experience “period like” discomfort that varies from patient to patient, as well as from one treatment cycle to another.

You may also experience some abdominal bloating. These symptoms are common, but please contact us with any concerns.



Q: Is it normal to have vaginal bleeding / spotting before my pregnancy test?

A: Vaginal spotting / bleeding can occur during your luteal phase of treatment and it doesn't necessarily mean that the treatment has failed and you are not pregnant.

This is why it is important to continue all medications prescribed to you until your pregnancy test. If you have any concerns, please call us.

Q: What can I take for constipation?

- Increased fluid intake.
- High fibre diet.
- If no relief “Lactulose” (according to product directions).



Please visit our PIVET website for a detailed listing of “frequently asked questions”

www.pivet.com.au

GYNAECOLOGICAL PROCEDURES

1. DILATATION & CURETTAGE



D&C, also known as *dilation and curettage*, is a surgical procedure often performed after a miscarriage or as a diagnostic procedure. Dilation means to open up the cervix; curettage means to remove the contents of the uterus.

Curettage may be performed by gentle scraping of the uterine wall with a curette instrument or by a suction curettage (also called vacuum aspiration), using a vacuum-type instrument. The tissue collected through this procedure can then be sent to a pathology centre to be analysed.

2. COLPOSCOPY

Colposcopy is an examination of the cervix using a colposcope (a microscope to check for abnormal cells). It magnifies the image so that any cervical abnormalities can be viewed more closely. Colposcopy is necessary when a cervical smear test result reveals an abnormal finding. This finding may not necessarily be due to cancerous cells, but may be caused by inflammation / infection. During the procedure, you will be asked to lie on the examination bed as you would when having a pap smear. A speculum is gently passed into the vagina allowing the doctor to view the cervix with the colposcope. The cervix will be cleaned and swabbed with a solution of either acetic acid (a weak vinegar solution) and/or an iodine solution so the doctor can clearly visualise the abnormal areas.

3. CERVICAL BIOPSY

During your colposcopy procedure, the doctor may think it is necessary to take a small biopsy of the tissue from any abnormal areas to aid diagnosis.

This will be sent to the laboratory for further testing. Following the procedure you may experience some slight spotting which can last up to a week. This procedure is generally attended to in the doctors rooms without sedation. If sedation is deemed necessary you may be booked for your procedure to be carried out in PDSC.



4. LLETZ PROCEDURE

A LLETZ procedure (Large Loop Excision of Transformation Zone) is required when abnormal cells are identified from your pap smear or from a cervical biopsy. This procedure is carried out in our day procedure unit (PDSC) under intravenous sedation. During the procedure, a colposcopy is performed (see above information) and a semi-circular wire loop is used to remove the area of the cervix in layers that contains the abnormal cells or changes. Diathermy is sometimes used to stop any significant bleeding. The procedure takes approximately 20 - 30 minutes including the sedation time. The removed area of cervix is sent to Clinipath pathology for further testing. You will be required to book a follow up appointment with your doctor in approximately 4 weeks to obtain these results and the type of follow up you will require.

5. ENDOMETRIAL BIOPSY

An endometrial biopsy is a procedure where a small sample of tissue is taken from the endometrium (lining of the uterus) and sent to Clinipath pathology to be examined under the microscope for tissue changes. This procedure can be performed as a diagnostic test for women that present with heavy bleeding or pelvic pain or it can be performed in the cycle prior to fertility treatment to help aid embryo implantation.

The procedure is can be performed in the doctor's rooms or PDSC without sedation. The doctor will insert a speculum into the vagina to visualise the cervix and then a small hollow plastic tube (called a pipelle) will be inserted through the cervix into the uterine cavity. Gentle suction is then used to remove a sample of tissue. Once this has been obtained, the sample will be sent off to the laboratory. Occasionally the use of other instruments are required if the procedure is not straight forward and your doctor may book you to have the procedure attended in PDSC under ultrasound guidance and/or with the use of sedation. There may be an additional cost on top of your consult fee for this procedure - please enquire with administration for charges payable on the day of your appointment.

6. INSERTION OF MIRENA

A Mirena is an intrauterine device containing the hormone Levonorgestrel which can be used as a contraceptive, to treat heavy menstrual bleeding and/or to protect the endometrium (lining of the uterus) as a part of hormone replacement therapy during menopause. It comprises of a small plastic frame with copper wire wrapped around the plastic and threads to assist removal. The Mirena can be either fitted in the doctors rooms at PIVET during consultation without sedation or alternatively your doctor may book you to have your procedure in the day procedure unit under sedation and ultrasound guidance. There may be an additional cost on top of your consult fee for this procedure - please enquire with administration for charges payable on the day of your appointment.



NB: You will be given a prescription for the device and must obtain it from the pharmacy prior to your procedure.

7. INSERTION OF IMPLANTS

After a hysterectomy, testosterone and estradiol implants are sometimes required. This procedure is performed in PDSC under local anaesthetic. After administration of anaesthetic, a small incision is made in the skin and an introducer is used to place the implant in the fatty tissue and the skin is sutured closed. There is an additional fee for the implant to be ordered (payable to the pharmacy prior to insertion) and a fee for the implant to be inserted, which is payable on the day of the procedure. Please enquire with Administration staff regarding the fees.

8. INSERTION OF ZOLADEX

Zoladex is an injection that is used for the treatment of endometriosis. Some women will require treatment with Zoladex following surgery to help improve their chances of conceiving. A course of Zoladex is generally prescribed for up to 6 months prior to embarking on an IVF treatment cycle. During this time you may also be prescribed an oral medication called Provera (Medroxyprogesterone acetate) to help further suppress your endometriosis, decrease the side-effects (similar to menopause) and prepare your body for treatment.

You will be required to see the doctor to obtain an authority prescription (if eligible) or a general prescription for the medication. After obtaining the Zoladex from the pharmacy, you will need to attend the clinic for a scheduled doctors appointment so that the injection can be performed. This is performed in the doctors rooms and takes approximately 5 minutes. You will be required to attend on a monthly basis until the Doctor decides its appropriate to cease treatment. This is determined by the doctor by ordering blood tests to monitor your progress and suppression of endometriosis.

PREGNANCY CARE

1. PREGNANCY SUPPORT AND EARLY PREGNANCY MONITORING

Once achieving a positive pregnancy result at PIVET, ongoing monitoring is recommended. At the time of a final blood test result you are approximately 4 weeks pregnant. You will be given a due date upon request to a clinic Nurse or Midwife which is calculated by various factors related to your treatment cycle. During pregnancy monitoring we perform blood tests and ultrasounds to determine fetal and maternal wellbeing.

Once you receive a pregnancy result it is often necessary to consider if you are wishing to deliver your baby at a public hospital or private hospital after being discharged from PIVET at 12 weeks of pregnancy. If you are wishing to book into a private obstetrician (refer to obstetrician list provided at your 5 week pregnancy blood tests for a list of consultants, private and public hospitals available in the Perth metro area), we encourage booking in no later than 6 - 7 weeks pregnant to avoid disappointment with your choice of obstetrician. Alternatively if you wish to go through the public system you can call your local hospital (refer to obstetrician list to see which catchment zone you fall into).

Pregnancy monitoring at PIVET comprises of the following:

- **5 weeks pregnant** - Blood test (E2, P4, β hCG).
- **6 weeks pregnant** - Blood test (E2, P4, β hCG + antenatal screen including; Antibody screen, random glucose, ferritin, Full blood count, Hepatitis B & C, thyroid function test and vitamin D). If there are any abnormalities with the results of your antenatal screen they will be discussed with you at your 7 week appointment by either the Midwife or Doctor.
- **7 weeks pregnant** - Blood test (E2, P4, β hCG), Ultrasound & Doctors appointment.
- **8 weeks pregnant** - Blood test (E2, P4, β hCG).
- **10 weeks pregnant** - NIPT blood test (Harmony blood test performed at Clinipath pathology) or First trimester screening blood test (you will not receive a results call from this blood test, as it is a combined test which will be discussed with you by the doctor after your ultrasound at your 12 week appointment). These options will be discussed with you at your seven week Doctors appointment and relevant referrals will be given.
- **12 weeks pregnant** - Ultrasound and Doctors appointment (discharge appointment from PIVET).



If bleeding occurs it is best to rest in bed and inform the nurses at PIVET. You may be commenced on Provera tablets (see below for additional information) that provide extra progesterone. If you are a negative blood group it is important to attend to see a doctor so an injection of Anti D can be administered.

SINGLETON PREGNANCY:

- i. You will be required to see a PIVET Doctor at 7 weeks to discuss the pregnancy and who will undertake your ongoing obstetric care after discharge from PIVET at 12 weeks. At this appointment, the doctor will discuss any support medication you may be taking and formulate a "weaning-off"

schedule for you. Any further follow up requirements from the antenatal screening bloods will also be discussed & planned at this time.

- ii. The doctor will instruct when you require your next visit. At each antenatal visit you will have your (a) blood pressure taken (b) weight recorded (c) urine tested.
- iii. We recommend all patients have a first trimester screening. This is to detect possible abnormal conditions e.g. Downs Syndrome. If the test reveals a positive result, this will be discussed with you and further testing may be offered. However depending on your moral or religious views you may not wish to pursue this test. It is our view that the blood test and scan be undertaken regardless.
- iv. PIVET will take your pregnancy care through until the 12th week, or the end of the first trimester. Please ensure that you have arranged for an obstetrician or a public hospital to take over your care from this time.
- v. Do **NOT** stop your hormone support therapy until instructed by the PIVET staff or at least discussed beforehand.

MULTIPLE PREGNANCY:

Multiple pregnancy can occur from the simultaneous release and fertilization of 2 or more ova (dizygotic multiple pregnancy) or from the early division of a fertilized single ovum (monozygotic twin). If you have a confirmed multiple pregnancy your future care will follow the same sequence of events as of the start of this information sheet. After your scan you will be instructed to:

- i. Commence taking Provera tablets to relax the uterus and reduce any uterine irritability.
- ii. An appointment will be made to see a PIVET doctor to discuss the pregnancy and your ongoing care.
- iii. The doctor will instruct you as to when your next visit needs to be booked. At each antenatal visit you will have your (a) blood pressure taken (b) weight recorded (c) urine tested.
- iv. A cervical suture may be discussed with you if the doctor thinks it may be of benefit to you. The suture is usually be inserted between 12-14 weeks gestation.
- v. Do **NOT** stop your hormone support therapy until instructed by the PIVET staff or at least discussed beforehand.

ADDITIONAL INFORMATION

MORNING SICKNESS:

As many of our patients are on pregnancy support, they may experience morning sickness for the first trimester of pregnancy. We do not recommend taking any drugs to reduce this. However, there are several measures that may reduce the sickness:

- eat small amounts of food rather than three large meals a day
- try to avoid acidic foods, such as fruit juices, fruit, vegemite, some vegetables
- eat mostly plain carbohydrate foods
- avoid dehydration and low blood sugar
- a sickness band worn on the wrist helps many of our patients

If morning sickness continues despite the above measures and you are unable to tolerate diet and fluids please contact the PIVET nursing staff for further instruction.

ABDOMINAL PAIN:

Often when pregnant for the first time, some pain is felt low in the pelvis. This is caused by the ligaments which support the uterus stretching as the uterus increases in size. It settles with bed rest and is not usually so noticeable in subsequent pregnancies. Any continuing abdominal pain should be reported. Should this occur, we ask you to telephone the nurses at PIVET if occurring during your first trimester (first 12 weeks), or your obstetrician if after this time.

CONSTIPATION:

This can be a common problem throughout pregnancy. Eating a high fibre diet and drinking plenty of water each day will help you maintain regular bowel habits. Natural aperients may be taken if absolutely necessary, but should be only very mild in action.

EXERCISE:

Providing all is well with your pregnancy and you have had permission from your doctor, it is advisable to keep yourself fit. Gentle exercise such as walking, swimming and aqua aerobics are advised.

LONG DISTANCE TRAVEL:

We advise against long distance travel and air travel during pregnancy. Please consult your doctor to discuss further.

Referral for care after 12 weeks:

After your 7 week appointment a referral letter to your obstetrician of choice or your local public hospital will be sent from PIVET detailing your history (medical and surgical) and a summary of your treatment and medications. Blood test results (including blood tests attended at 6 weeks, rubella, pap smear result, blood group and any other relevant blood test results) and your 7 week ultrasound result will be sent along with your referral letter. Please note as we are a specialist facility our referral to your obstetrician or public hospital is only valid for 3 months and therefore you will be required to obtain a referral from your General Practitioner to continue your care for the remainder of your pregnancy.

2. THE USE OF DRUGS AND HORMONES FOR SUPPORT DURING PREGNANCY

There are a number of instances where it may be appropriate to supplement a pregnancy with hormones:

1. At PIVET Medical Centre, we monitor pregnancies for the first eight weeks. This is done by weekly blood tests, where we assess oestrogen, progesterone and β hCG levels, along with ultrasound scans. If the clinical team finds that any of the hormone levels are at a suboptimal level for the stage of pregnancy, they may wish to supplement these by administering them in a tablet, injection or pessary form.
2. In cases where there has been a history of recurrent miscarriage, the clinical team will normally administer support hormones (oestrogen, progesterone, medroxyprogesterone acetate, human chorionic gonadotrophin [β hCG]). This is to help maintain the pregnancy and reduce the risk of further miscarriage.
3. There are a number of women who have suboptimal hormone levels in their natural menstrual cycle. In these cases, the clinicians may administer oestrogens and progesterone or other drugs in order to create a menstrual cycle suitable for the transfer of embryos. These are termed Hormone Replacement Therapy (HRT) cycles. When a pregnancy is achieved during an HRT cycle, it is important that the oestrogens and progesterones are continued into early pregnancy.

The support hormones used at PIVET Medical Centre have been carefully investigated to ascertain their usefulness and side effects during pregnancy. General medical advice would indicate that the administration of any drugs, chemicals or hormones during pregnancy should be avoided.

This is to decrease the risk of any abnormality in the developing embryo and foetus. We have monitored the use of these support hormones over many years and have found no clinical or reported adverse effects on the developing embryo and foetus.



The support hormones that may be administered during pregnancy at PIVET Medical Centre include:

1. **Pregnyl** – This is a form of human chorionic gonadotrophin (hCG). hCG is a natural hormone produced by the placenta and acts on the corpus luteum in the ovary to produce oestrogen and progesterone, which are involved in maintaining the lining of the uterus and the pregnancy. Pregnyl is administered in the form of a subcutaneous injection.

Side effects to Pregnyl may include headaches, irritability, restlessness, depression, nausea, vomiting, fatigue, swelling and mild pain at the site of injection.

2. **Progynova** – This product contains oestradiol valerate. It is normally used as part of HRT for the treatment of complaints and symptoms associated with the onset of menopause and other low oestrogen states. It replaces the hormone oestradiol that the woman is no longer producing and therefore can relieve symptoms such as hot flushes, sweats, sleep disturbances, nervousness, irritability and vaginal dryness. In addition, it is also used for preventing bone disease in later life. It is administered as oral tablets.

Side effects of Progynova include changes in vaginal bleeding pattern and abnormal bleeding or flow, breast tenderness and enlargement, dyspepsia (indigestion), nausea, vomiting, rashes and other skin disorders such as acne, headaches, migraine, dizziness, anxiety, depression, fatigue, changes in body weight and hypersensitivity reactions. In addition, oestrogens are known to increase the incidence of some forms of cancer, such as endometrial cancer, breast cancer and liver tumors. You should ensure that you discuss the use of this drug with your doctor at PIVET Medical Centre prior to use.

3. **Progesterone and Combined Oestrogen / Progesterone pessaries** - This is a progesterone product in a pessary form. It is preferably inserted into the vagina, but if instructed to, may also be used by insertion into the rectum. The pessaries are indicated as luteal support during fertility treatment and may be increased throughout the cycle or pregnancy if there is a progesterone deficiency.

Pessaries are not used where there is undiagnosed vaginal bleeding, undiagnosed urinary tract bleeding, liver dysfunction or disease and thromboembolic disorders. Animal studies have shown that some synthetic progestogens may induce and/or promote formation of certain types of cancer. The clinical relevance of this to humans is unclear. Where progesterone levels are insufficient as in assisted reproductive procedures, progesterone pessaries have been successfully used to support embryo implantation.

Side effects to these pessaries may include amenorrhoea, hyperglycaemia and skin rashes.

4. **Provera** - This is a substituted progesterone in the form of medroxyprogesterone acetate. Provera is prescribed for endometrial carcinoma, endometriosis and secondary amenorrhoea. It has actions comparable to progesterone and induces glandular maturation in the endometrium, maintains pregnancy, and inhibits ovulation. It is administered as an oral tablet.

Although Provera is categorised as a progestogen it is different from almost all the others in this category because it is produced from progesterone, unlike the others which are derived from testosterone and are absolutely contraindicated in pregnancy. We have trialled Provera extensively at PIVET and published reports showing that there are no harmful effects on the developing fetus or any significant problems for the mother whilst taking these medications.

Provera is used with caution in patients with histories of thrombotic disorders (blood clots of various organs or vessels of the body) including stroke (cerebrovascular accident). It is contraindicated where there is impaired liver function, undiagnosed vaginal bleeding, missed abortion and hypertension, and endometrial, renal or breast cancer. As Provera may cause some degree of fluid retention, conditions such as epilepsy, migraine, asthma or cardiac or renal dysfunction may be exacerbated by its use.

Side effects of Provera may include hypersensitivity, thrombotic disorders, nervousness, insomnia, depression, dizziness, headaches, rashes, acne, hirsutism, irregular uterine bleeding and spotting, nausea, breast tenderness, moderate elevation of blood pressure and weight gain.

5. **Cardiprin** – This substance (*aspirin*) taken orally in tablet form has antiplatelet and antithrombotic effects (i.e. acts in preventing blood clots).

Cardiprin is contraindicated in cases of severe liver disease or renal damage, haemophilia or other bleeding disorders or where there are peptic ulcers. Animal studies have shown that aspirin can cause birth defects in some species. There is no firm evidence that aspirin produces malformations in humans.

Side effects of cardiprin may include epigastric distress, nausea, vomiting, activation of peptic ulcers, dizziness, temporary deafness and metabolic disorders. As cardiprin is a low dose aspirin, side effects are minimised.

3. BLEEDING IN PREGNANCY

Vaginal bleeding in pregnancy can be very common particularly following a treatment cycle. Depending on the stage you are in your pregnancy and the amount will determine the management of your bleeding. The staff at PIVET understand that this can be a stressful time and are here to help you deal with your anxieties. **Please contact a PIVET nurse at the onset of any bleeding during your pregnancy.**

As a general rule, if you are under 12 weeks pregnant and you have bright red bleeding that is greater than the size of a 20 cent piece in your underwear, you may be required to attend the clinic for a review with the Doctor. Sometimes the nursing staff will arrange an ultrasound prior to you seeing the doctor if you are over 7 weeks pregnant. Provera is a medication that is commonly used in pregnancy to treat bleeding (please see information above on Provera and its use).

If the bleeding is brown, dark brown or pink in colour it is generally nothing to be too concerned about and the nurses will just advise you to rest and monitor the vaginal loss.

If you are a negative blood group you may be required to attend the clinic for an injection of Anti-D within 72 hours of any bleeding. This is due to the possibility of the baby's red blood cells possibly crossing the placenta into your bloodstream. If this occurs and your baby has a positive blood group your immune system can produce antibodies against the baby's blood cells. These antibodies may not necessarily affect your current pregnancy but may lead to serious complications in future pregnancies with babies with positive blood groups. If you are unsure of your blood group please contact the nurses at PIVET to find out.

It is very important to continue all your prescribed medication, unless you are advised otherwise by a PIVET Doctor or Nurse.

4. RECURRENT PREGNANCY LOSS SUPPORT

In circumstances where women have undergone two or more consecutive pregnancy losses it may be appropriate to offer women additional hormonal support. To arrange these additional medications you will be advised to book an appointment with one of the doctors between 4 - 5 weeks pregnant to discuss these medications, sign a consent for their use and to obtain prescriptions.

The schedule consists of:

- **Pregnyl 5000IU** - subcutaneous injection twice a week until 12 weeks.
- **Provera 20mg** - orally four times a day from 5 - 16 weeks.
- **Cardiprin 100mg** - orally until 35 weeks or at discretion on obstetrician.

Additional medication may include:

- **Prednisolone 5mg** - orally twice a day until 12 weeks.
- **Progesterone 400mg, 500mg or Combined (Oestradiol & Progesterone) pessaries** - daily to five times a day depending on individual patient requirements. Pessaries continue until 12 weeks.
- **Clexane 20mg** - Subcutaneous injection daily until 12 weeks.

5. PREGNANCY LOSS

Unfortunately pregnancy loss can affect approximately 1 in every 5 pregnancies and majority of these occur within the first 8 weeks of pregnancy. Approximately 50% of pregnancy losses are due to chromosomal problems with the fetus.

Miscarriage

A miscarriage is defined as the loss of a pregnancy prior to 20 weeks gestation. Miscarriages can be complete or delayed. A complete miscarriage often involves heavy vaginal bleeding and/or passing of clots or tissue. This more commonly occurs in spontaneous pregnancies or treatment cycle generated pregnancies where no hormonal support is being used.

Delayed miscarriage is more common in this setting due to the additional pregnancy support hormones that patients are commonly prescribed. Delayed miscarriage is when a pregnancy has stopped developing but without any pain or bleeding. Typically this would be diagnosed on ultrasound however you may have been given some indication from the clinic nurses that your weekly pregnancy hormone level (β hCG) has not been rising as expected.

If you have a history of multiple miscarriages the doctor may advise additional blood tests to further investigate the cause of your pregnancy loss. These blood tests can include testing for Toxoplasmosis, CMV, NK cells, Thrombophilia screen, $\alpha\beta$ GP-1 antibodies, Brucellosis, MTHFR gene.

These tests may incur an out-of-pocket cost up to \$300.

Biochemical Pregnancy

A biochemical pregnancy occurs when a pregnancy does not continue to develop after the final blood test and upon return for your follow up blood test at week 5 or 6 the pregnancy hormone has returned to a non-pregnant level (<10). If this occurs you will be advised to cease any support medication you are currently taking and you can expect a period within 10 days of ceasing your support medication.

Ectopic Pregnancy

An ectopic pregnancy is one that develops in the fallopian tube rather than in the uterus. While this can be potentially a very dangerous situation due to the extensive pregnancy monitoring carried out at PIVET the risk of you being in any serious danger is minimal. You may be given some indication that the Doctors suspect an ectopic pregnancy as a result of your weekly hormone levels when contacted by nursing staff with results. Typically an ectopic pregnancy presents with low rising pregnancy hormone levels. Please report to nursing staff if you experience any sharp pain or bleeding.

It is very important to continue all prescribed medication unless advised otherwise by a doctor. If you are diagnosed with an ectopic pregnancy after your 7 week ultrasound you will be advised regarding the appropriate management. Sometimes this may involve a laparoscopy to remove the fallopian tube or alternatively you may be offered an injection of methotrexate to stop the embryonic cells from dividing and multiplying as a non-surgical method of ending pregnancy in its early stages. Your Doctor will discuss with you which option is more appropriate to your clinical situation.

Suction Dilatation and Curettage (D&C)

For all women who have been diagnosed with a delayed or partial miscarriage at PIVET it will be recommended to undergo a Dilatation and Curettage (D&C). A suction D&C is a procedure carried out under sedation and involves the use of a suction device to evacuate the contents of the uterus followed by a gentle

scrape to ensure the entire pregnancy has been removed. The tissue that is removed is then sent off to the laboratory to be analysed for chromosomal abnormalities (cytogenetics).

Following your D&C you will be required to attend follow up blood tests to ensure your pregnancy hormone returns to a normal (non-pregnant) level. This may take a few weeks depending on how advanced your pregnancy was at the time it demised and you be advised accordingly from nursing staff regarding your required attendance. It is recommended you book a review appointment with a Doctor approximately 1 month following your procedure to obtain your cytogenetic results and to check your recovery following the procedure. You may wish to also discuss or set up further treatment at this time.



AFTER HOURS CARE

Dealing with Problems After Hours

The information below has been provided to assist you in what to do with problems you may be having after hours. WADMS is an after hours service you can access in situations where you are required to obtain a consultants advice. Please use the chart below as a guide to what action needs to occur should you encounter these problems outside of clinic hours.

WADMS Contact Number: 08 9321 9133

Bleeding	Call WADMS	Call PIVET Nurse next day	Further Information
During treatment cycle.	No	Yes	Continue any drugs you are currently taking until further notice from nursing staff.
Heavy, bright vaginal bleeding following egg collection.	Yes	No	
Spotting or bleeding prior to final blood test (pregnancy result).	No	Yes	Continue all current support drugs until final blood test. This is not indicative that you will receive a negative pregnancy result.
Spotting during pregnancy.	No	Yes	If you are a negative blood group, please ensure you call a nurse to discuss if it is required to attend for an Anti D injection.
Heavy bleeding during pregnancy.	Yes	No	See above comment.
Heavy bleeding following dilatation and curettage (D&C) or colposcopy.	Yes	No	

Pain, Shortness of Breath & Vomiting	Call WADMS	Call PIVET Nurse next day	Further Information
Prior to or after egg collection.	No	Yes	Paracetamol 1g six hourly, rest, heat packs and maintain fluids.
Severe pain prior to or after egg collection.	Yes	Yes	As above.
Cramping (period like pain) during pregnancy.	No	Yes	Some mild cramping may be normal in early pregnancy. Use paracetamol and heat packs as needed.
Intermittent or continuous pain localised to one side during pregnancy.	Yes	No	
Shortness of breath before or after an egg collection.	Yes	No	
Vomiting prior or after egg collection.	Yes	No	Maintain fluid intake.

Drug / Medication issues	Call WADMS	Call PIVET Nurse next day	Further Information
Insufficient pessaries to last until next clinic visit.	No	Yes	Continue current regime of drugs (DO NOT STOP) if more required urgently and its outside of clinic hours, contact Wembley Pharmacy to check if a repeat prescription available to collect until checking with nursing staff the next day.
Insufficient Puregon or Gonal F available for next dose.	No	Yes	Administer the maximum of what is available in your pen device & speak to a clinic nurse once clinic re opens.
No drug available for trigger dose that night.	Yes	Yes	
Water vial shatters prior to drawing up to use for mixing Pregnyl.	No	Yes	Purchase 1ml of Water for Injection from your local pharmacy or Wembley Pharmacy.
Insufficient needles / syringes for evening injection.	No	Yes	Purchase from your local pharmacy.
Query regarding injection technique, despite watching instructional DVD or reading information included with injection device.	No	Yes	

Results	Call WADMS	Call PIVET Nurse next day	Further Information
Insufficient pessaries to last until next clinic visit.	No	Yes	Continue current regime of drugs (DO NOT STOP) if more required urgently and its outside of clinic hours, contact Wembley Pharmacy to check if a repeat prescription available to collect until checking with nursing staff the next day.
Insufficient Puregon or Gonal F available for next dose.	No	Yes	Administer the maximum of what is available in your pen device & speak to a clinic nurse once clinic re opens.
No drug available for trigger dose that night.	Yes	Yes	
Results from initial screening blood test attended after initial appointment.	No	No	Generally no new is good news. If anything requires follow up a nurse will contact you to let you know what is required or to attend to discuss further with the doctor. Alternatively you are welcome to book an appointment to discuss your results with the Doctor prior to your next scheduled appointment.
Results not obtained from blood test and ultrasound performed that day.	No	Yes	If you are currently taking any drugs continue the same regime until you have spoken to a nurse. Call clinic nurse when clinic opens then next morning.

Pregnancy	Call WADMS	Call PIVET Nurse next day	Further Information
Unsure of embryo transfer time.	No	Yes	Call clinic as soon as open the next day to obtain your time for the next day.
Fertilisation results.	No	No	Contact PIVET and ask to speak to an embryologist for results.
Cramping (period like pain) during pregnancy.	No	Yes	Some mild cramping may be normal in early pregnancy. Use paracetamol and heat packs as needed.
Intermittent or continuous pain localised to one side during pregnancy.	Yes	No	
Spotting during pregnancy.	No	Yes	If you are a negative blood group please ensure you call a nurse to discuss if it is required to attend for an Anti D injection. If you are unsure of your blood group please contact a member of nursing staff to check.
Heavy bleeding during pregnancy.	Yes	No	If you are a negative blood group please ensure you call a nurse to discuss if it is required to attend for an Anti D injection.
Severe nausea and vomiting associated with dizziness.	Yes	No	Maintain fluid intake where appropriate.

DONOR SERVICES

1. TYPES OF DONATION

Unknown Donation

Unknown donors are people that have either contacted the clinic to donate gametes (eggs/sperm) or embryos or may have responded to clinic advertising for donors. The identity of these donors is kept confidential. To access unknown donation through PIVET you will be required to see a Doctor to discuss your requirements and suitability. There is a “waiting list” to access unknown donated gametes/embryos.



Known Donation

Known donors attend the clinic with their recipients, who are often already PIVET patients. Known donors can be related in some instances (e.g. a sister donating eggs to their sister or brother donating sperm to their brother). Known donors do not have to be related, they can be friends or even acquaintances, but their identity is “known” and contact has been made. **The rules governing “known” donation differ in that there is a mandatory “cooling off” period which must be observed in all cases of known donation - this cannot be waived.**

2. DONOR SPERM

Donor sperm is used either for an intra uterine insemination (IUI), IVF or ICSI treatment cycle. The treatment cycle is determined by the clinician following assessment and investigation of fertility requirements. In the case of single females or same sex couples this assessment is a necessity prior to accessing donor sperm. Single females and same sex couples cannot access IVF/ICSI procedures on the basis of social infertility. When a treatment cycle has been determined, donor profiles, with non-identifying characteristics are offered to recipients.

Note – More than one recipient, but no more than five, will benefit from each unknown donor.

Under West Australian Law, sperm may be stored for a maximum of 15 years, at which time it must be removed from storage and allowed to succumb. Under exceptional circumstances the storage period may be extended following application to the Reproductive Technology Council. Donated sperm cannot be used after the death of the donor.

3. DONOR EGGS

Donor eggs are used for the purpose of achieving a pregnancy for a woman who is medically unable to produce her own suitable eggs or where there is a genetic contraindication. The donor may be unknown or known to the recipient/s of the eggs. Donor profiles, with non identifying characteristics, are offered to recipients.

Note – Usually more than one recipient (but no more than five) will benefit from each unknown donation. Depending on the number of eggs collected we aim to direct four eggs to each recipient.

Under West Australian law eggs may be stored for a maximum of 15 years, at which time they must be removed from storage and allowed to succumb. Under exceptional circumstances the storage period may be extended following application to the Reproductive Technology Council. Donated unfertilised eggs cannot be used after the death of the donor.



4. DONOR EMBRYOS

Donor embryos are normally used when the woman is medically unable to produce her own eggs and the male partner is infertile or the couple have been unable to achieve a pregnancy following fertility treatment. Due to the shortage of donor oocytes, many women / couples may choose donor embryos to achieve a pregnancy. The embryos normally arise from couples who wish to donate their stored (frozen) embryos following the completion of their treatment. Donor profiles, with non-identifying characteristics, are offered to recipients.

Note: Sometimes more than one recipient (but no more than five) may benefit from each unknown donation depending on the numbers of embryos available.

Under West Australian Law, embryos may be stored for a maximum of 10 years, at which time storage period may be extended following application to the Reproductive Technology Council.

The destiny of donated embryos following death of the donor(s), in the absence of clear direction from the donor(s), would be assessed on an individual basis.

5. DONOR WAIT LISTS

CHOOSING A DONOR

Choosing a donor is one of the most challenging decisions you will ever make

- Give yourself time to grieve your loss of a genetic connection to your child.
- Give yourself time to move forward and appreciate the options available through medical innovations.
- Take the time to realize that you (and your partner) are creating a child who is unique to your family and would not be created if not for your love for each other.
- Remember that blending the genetics of any two people will bring an unpredictable outcome in a child, a child that will be cherished regardless of hair colour or sporting achievement.
- Read about the characteristics of the donor and choose someone you can relate to.
- Choose someone who feels like a fit with your family.
- Make sure you are comfortable going ahead with treatment – there is extra counseling available should you feel you need it.



To quote Gail Sexton Anderson - Donor Concierge

“Don’t become overly fixated on any one characteristic that you want in a donor. Each person is unique; look for qualities in the donor that appeal to you but don’t try to reproduce yourself. Even when parents deal with their own genetics, they never know what surprises they might see in their children.

No matter how a child is brought into this world, we love them for both their similarities to ourselves and their differences.”

“However your child comes to join your family, you will love your child no matter what; they are the child you were destined to have.”

6. PSYCHO-SOCIAL COUNSELLING



Counselling is available from PIVET's *Approved (Fertility) Counsellor* who has experience in all aspects of infertility and reproductive health issues. It is PIVET policy that all patients accessing anonymous donor material have at least one counselling session prior to any treatment to consider the implications for them the donor conceived child. Follow up counselling is available if the need arises.

Information regarding the medical, personal and social implications of rearing donor children is also available from:

- Reproductive Technology Council - <http://www.rtc.org.au>
- Donor Conception Support Group - <http://www.dcs.org.au>

In the case of **known donation** all parties (donor & partner if any, recipient & partner if any) must attend counselling sessions at the beginning and conclusion of the mandated "cooling off" periods.

The "cooling off" period is 6 months for sperm donation (this can run concurrently with the quarantine period) and 3 months for eggs and embryo donation (*which occurs prior to the commencement of the donor's treatment*) (HRT Act Directions 5.8 & Part 2 Schedule 4).

7. QUARANTINE & SCREENING

All sperm, egg and embryo donors have a clinical consultation with a doctor and they are required to complete a *Family Medical History Form* detailing an extensive list of genetic conditions. They also have blood tests for a number of diseases and conditions (listed below).

The tests include the following:

- Karyotype: all donors must have normal number and arrangements of chromosomes
- Cystic Fibrosis: for 10 of the most common gene abnormalities Ile507del (Δ I507), Phe508del (Δ F508), 489+1G>T (621+1), Gly542X (G542X), Gly551Asp (G551D), Arg117His(R117H), 1585-1G>A (1717-1), Trp1282X (W1282X), Asn1303Lys (N1304K) and Arg553X (T553X)
- HIV I & II antibody
- HTLV I & II antibodies
- Syphilis
- Chlamydia
- Gonorrhoea
- Hepatitis B surface antigen + core antibody
- Hepatitis C antibody



Donors are also screened for ethnically related diseases, where appropriate:

- Mediterranean or Asian heritage - **Thalassaemia**
- African heritage - **Sickle-cell anaemia**
- Jewish heritage - **Tay-Sachs and Gaucher's disease**

Donated sperm, eggs, embryos and embryos generated from donated eggs, are routinely quarantined for a minimum of six (6) months. The donor is then requested to attend for a final blood test, the results of which will satisfy quarantine requirements and the gametes / embryos made available for use in treatment.

Unknown donations have been cleared from quarantine prior to being offered to recipients.

8. RESIDUAL RISKS

Despite the level of screening performed, there are still risks associated with the treatment, as there are many other genetic diseases that are deemed to be at too low risk for testing or the technology is not yet available for testing. If pregnancy should result from the treatment, we cannot rule out the possibility of physical, mental or psychological abnormalities to the child from an unsuspected hereditary illness.

If a genetic disorder is declared by a donor, the recipient may wish to make an appointment with our Genetic Counsellor to discuss the risks of inheritance of this disorder in relation to the background general population risk.

It should be noted that the risk of chromosomal abnormalities increases with the age of the female donor (as in the case of egg donors), and that there are higher miscarriage rates and lower successful implantation rates in higher age groups for recipients.

9. GENETIC COUNSELLING

It is a PIVET policy that all unknown donors undergo genetic counselling prior to gametes / embryos being released for use. All recipients are *strongly encouraged* to consult with PIVET's Clinical Geneticist prior to a treatment cycle where donated gametes / embryos are being utilised.

10. REGULATION & THE LAW

The *Artificial Conception Act of 1985* protects the donor from any legal responsibilities or rights to any children born as a result of the donations, and any child born automatically becomes the legal child of the woman delivering or couple involved. This is the case for treatment of single women and couples (married, de facto, same sex).

In relation to a child born as a result of donation, all records are confidential to the clinic and the Reproductive Technology Registers held by the WA Department of Health and identifying details are kept securely. The care of the child is the legal responsibility of the couple who consent to the donation procedure, and the husband or partner (in a defacto situation), if any, is the legal father of the child.



Confidential identifying and non-identifying information about all donors, recipients, and children born as a result of donor treatment is supplied to the Reproductive Technology Registers held by the WA Department of Health <http://www.rtc.org.au>. Under the Human Reproductive Technology Act (1991) Amendment 1, December 2004 any child born as a result of egg / sperm or embryo donation on reaching the age of 16 years will have access to identifying information about the donor, following approved counselling. This process may be facilitated by the Reproductive Technology Unit and clinics.

For children under the age of 16 years each donor and recipient needs to consent to sharing identifying information and the parent needs to consent on behalf of the child. There must be approved counselling of all parties (which may include the child). All parties involved in donor conception (donors, parents of donor conceived children and donor conceived children over the age of 18 years), can register on the Voluntary Register where they may be able to access identifying information.

This depends on whether the other parties are also registered and their instructions on information to be made available. The Voluntary Register website is: www.voluntaryregister.health.wa.gov.au.

11. KNOWN DONOR CHECK LISTS

The below check lists have been designed to assist you and your known donor with fulfilling all the appropriate requirements prior to proceeding with treatment.

No.	<p align="center">KNOWN SPERM DONOR CHECKLIST</p> <p align="center">It is the responsibility of the recipient to ensure all requirements are met. Please note No. 2-5 can be attended on the same day to minimise your visits to the clinic.</p>	DATE ATTENDED	✓
1	GP referral required		
2	Consultation with PIVET Clinician		
3	Blood Tests for Initial Screening - attended directly after consultation with PIVET Clinician (no appointment necessary)		
4	Counselling (to commence “cooling off” period of 6 months) - book through PIVET reception. An individual and a combined appointment with your recipients on the same day is required to complete this process.		
5	Initial semen Analysis - book through PIVET reception		
6	Ultrasound - book through SKG and attend at least 2 days prior to review appointment (No. 8)		
7	Consultation with PIVET Clinical Geneticist - book through PIVET reception (at least 2 weeks following initial blood tests)		
8	Review appointment with PIVET Clinician to review blood test - book through PIVET reception		
9	<p>Sperm samples for freezing - please book appointments through PIVET reception with a minimum gap of 3 days between each sample. Please inform staff that you are a donor attending to ‘freeze’ a sample.</p> <p>Sample 1 <input type="checkbox"/> Date: _____</p> <p>Sample 2 <input type="checkbox"/> Date: _____</p> <p>Sample 3 <input type="checkbox"/> Date: _____</p> <p>Sample 4 <input type="checkbox"/> Date: _____</p> <p>Sample 5 <input type="checkbox"/> Date: _____</p> <p>You will be guided by PIVET lab staff regarding the amount of samples you will be required to produce.</p>		
10	Counselling (to close “cooling off” period of 6 months) - book through PIVET reception 6 months after initial counselling appointment. An individual and a combined appointment with your recipients on the same day is required to complete this process.		
11	Final blood test required to clear samples from quarantine - 6 months after last sample produced		

- ◆ Cooling off period for known sperm donation is 6 months (180 days).
- ◆ Cooling off and quarantine for sperm donation can be served concurrently.
- ◆ Additional sperm samples for quarantine are required following initial semen analysis (the analysis uses all the initial sample).

No.	<p align="center">KNOWN EGG DONOR CHECKLIST</p> <p align="center">It is the responsibility of the recipient to ensure all requirements are met. Please note No. 2-5 can be attended on the same day to minimise your visits to the clinic.</p>	DATE ATTENDED	✓
1	GP referral required		
2	Consultation with PIVET Clinician		
3	Blood Tests for Initial Screening - attended directly after consultation with PIVET Clinician (no appointment necessary)		
4	Counselling (to commence “cooling off” period of 3 months) - book through PIVET reception. An individual and a combined appointment with your recipients on the same day is required to complete this process.		
5	Ultrasound - book through SKG and attend at least 2 days prior to review appointment (No. 8)		
6	Consultation with PIVET Clinical Geneticist - book through PIVET reception (at least 3 weeks following initial blood tests)		
7	Review appointment with PIVET Clinician to review blood test - book through PIVET reception		
8	Counselling (to close “cooling off” period of 3 months) - book through PIVET reception 6 months after initial counselling appointment. An individual and a combined appointment with your recipients on the same day is required to complete this process.		
9	Donor “Day 21” appointment (to set up cycle and provide consents)		
10	Recipients “Day 21” appointment (to obtain consents and costing)		
11	Day 2 - Donor to commence treatment		
12	Egg collection → Embryos created → Quarantine commences		
13	Final blood test required to clear samples from quarantine - 6 months after last sample produced		



Cooling off period for known egg donation is 3 months (90 days).

12. COSTING

Please be aware that the cost of anonymous donated gametes / embryos **is not included** in the treatment cycle fees.

For known donation it is the responsibility of the recipient to absorb all out of pocket expenses for their donors.

Please ensure that you arrange a meeting with the finance department so you are fully aware of the costs involved **prior to commencing any treatment** with the clinic.



1. SURROGACY AT PIVET

The *Surrogacy Act 2008* (Act) commenced on 1 March 2009. The Act allows Surrogacy in certain prescribed circumstances. While the number of couples who may need to consider Surrogacy is small, being able to have a baby through Surrogacy when other options are not possible is important. There are strict requirements of participants before a Surrogacy arrangement can be approved by the Reproductive Technology Council.

A Parentage Order can only be made by the Family Court if the arrangement was approved by the Council. These may appear onerous and expensive but are important if the community is to feel comfortable with the process and to ensure all participants are equally supported. This information will outline some of the key aspects of Surrogacy and help you ask the right questions during your management



2. WHAT IS SURROGACY - DEFINITIONS

The new Act defines the commissioning couple as the **Arranging Parent(s)** and the Surrogate as the **Birth Mother**. These definitions will be used throughout the brochure and during your management at PIVET. **Altruistic Surrogacy** means it is an offence for a person to enter into a Surrogacy arrangement that is for reward. The intention is that the birth mother should not receive material benefit or advantage because of her involvement in the Surrogacy arrangement. *“Reasonable expenses” associated with pregnancy such as medical expenses, private health insurance, life insurance are permitted.*

The **RTC** is the Reproductive Technology Council of Western Australia, the body responsible for approving all Surrogacy arrangements. The **Parentage Order** is issued by the Family Court to allow the legal transfer of parentage. This transfers the responsibility of the child(ren) from the Surrogate (Birth Mother) to the Arranged Parent(s).

There are two types of Surrogacy:

- **IVF Surrogacy (or Gestational Surrogacy)** where the embryos are generated from gametes of the arranged parents or in some cases donated sperm or eggs. The Surrogate does not contribute her eggs and therefore has no genetic connection to the child. *Donor gametes (eggs/sperm) can only be used in a Surrogacy arrangement when the donor is available to be involved in the proceedings i.e. unknown donation not possible.*
- **Traditional Surrogacy** where the embryo is generated from using sperm from the male partner of the **Arranged Couple (or Donor)** and the Surrogate contributes her own eggs. IVF or AI may be used to generate the pregnancy.

An arrangement involving the use of the birth mother's egg can be more complex. In general, other Australian states offering Surrogacy do not offer *Traditional Surrogacy*. PIVET prefers IVF Gestational Surrogacy but will consider Traditional Surrogacy.

3. WHO MAY BENEFIT FROM SURROGACY?

Couples considering entering into a Surrogacy arrangement must have an appropriate medical reason for progression to Surrogacy. Examples such as an absent or structurally abnormal uterus that has resulted in cases of recurrent miscarriages or repeated IVF failure if supported by appropriate medical documentation. Medical conditions such as severe renal disease, unstable diabetes, severe cardio-vascular diseases or respiratory diseases such as Cystic Fibrosis.

Some immunological disorders (e.g. systemic lupus erythematosus) or dangerous haematological disorders may mean Surrogacy is appropriate. All such medical cases require supporting evidence from a Specialist medical referral.

PIVET will have to consider whether underlying diseases of the arranged parents are compatible with reasonable longevity before progressing with Surrogacy as below.

4. WHO CAN ACCESS SURROGACY AND WHO CAN BE A BIRTH MOTHER?

Am I eligible to access Surrogacy?

The Arranged Parent(s) must fulfil eligibility criteria as currently defined in Section 23 of the HRT Act 1991 **i.e. menopausal women and most menopausal women where menopause is not considered to be premature cannot be considered.**

The interests of the potential child will always be paramount in PIVET's considerations. This means that we also have to consider health and longevity aspects of the Arranged Parent(s) and the existing family setting to be satisfied that any children arising from Surrogacy will be born into a satisfactory family environment with parental nurturing to at least age 18 years. Medical conditions that may support the use of Surrogacy need to be viewed in this light. This may lead to an equal opportunity challenge.

Am I eligible to be a Birth Mother (Surrogate Mother)

There are a few restrictions on who may be a Birth Mother under the Act. If you are over 25 years of age and healthy (to carry a pregnancy) as assessed by a medical practitioner, then you may be suitable to be a Birth Mother.

5. INFORMATION FOR THE ARRANGED PARENTS

How do I find a Surrogate?

The Arranged Parent(s) will need to source their own Birth Mother. PIVET cannot facilitate this except to keep a Register of women who have expressed interest in acting as Birth Mothers. PIVET believes an optimum Surrogate (Birth Mother), in the setting of altruism, would ideally be a sister, close relative or long-standing close friend (e.g. school friend) of the Arranged Parent(s). In the absence of such candidate, Arranged Parents may be able to source a potential Birth Mother via personal advertisement.

One critical parameter in finding a Surrogate is that the arrangement must be altruistic. This means that the Birth Mother must not be acting for any financial reward. There are major penalties outlined in the Surrogacy Act for both the intended Birth Mother and Arranged Parents, as well as any introducing broker or agent if reward is given or offered. However, the Arranged Parent(s) can cover medical costs and other reasonable expenses and these are precisely described in Part 2, Division 1, and Section 6 to 11 of the Surrogacy Act. Specific Health, Disability or Life Insurance would be viewed as a reasonable expense as defined in the Act.

Costs

An initial administration fee is charged for the preparation of the Surrogacy application and associated Counselling. This fee is non-refundable, irrespective of the outcome. The Arranged Parent(s) are responsible for the out of pocket expenses incurred by the Surrogate (and if applicable, her partner). Following a successful application for approval of the arrangement by the RTC there will be additional costs for IVF egg collection, Vitrification and transfer(s). Obstetric costs will also be incurred. Please note that any IVF related procedures used in a Surrogacy arrangement are not subsidised by Medicare. If not already provided please contact our Administration Staff who will provide you with a costing sheet.

What is the process for transferring our embryos to a Surrogate?

Before your embryos can be transferred to your Surrogate, you will need to have approval to proceed with a Surrogacy arrangement from the RTC. The Surrogacy Act (2008) stipulates the process that must be followed before they will consider the granting approval. The process is as follows;

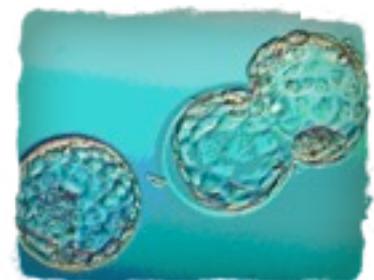
- Careful **medical evaluation of the Arranged Parent(s)** to ensure suitability (Section 23 of HRT ACT) and of any donors (erased donor's partners as not required).
- Careful **medical evaluation of the potential Birth Mother** (must be suited to carry a pregnancy) and medical evaluation also of any donors.
- **Counselling** to discuss the many and varied implications of *Surrogacy* with an Approved (Fertility) Counsellor at PIVET. Any dependent children of either party may also be required to participate in the counselling process.
- **Independent Psychological Assessment** of each member (Arranged Parent and Birth Mother and as applicable their partner's). This will be arranged after the Initial Counselling episode at PIVET. The group members will be referred outside PIVET for Psychological Assessment by a Clinical Psychologist.
- The completed **"cooling off period"** (Section 17) - i.e. at least 3 month before the approval is sought from the RTC each of the parties involved in the arrangement have:
 - Undertaken implications counselling.*
 - Been assessed by a Psychologist. This is confirmed in a written report.*
 - Have received independent legal advice about the effect of the surrogacy arrangement.*
 - Each of the arranged parents, birth mother and any donor has been assessed by a medical practitioner and confirmed in a medical report provided to Council to be medically suitable to be involved in a surrogacy arrangement.*
- Development of **legal documentation arrangements** and **reciprocal insurance cover**. The legal arrangements need to cover issues including which costs will be met by the Arranged Parents and the level of reimbursement of costs associated with the arrangement to the Surrogate. The law defines reimbursement that is allowed. Any additional payments are illegal.

Application to the RTC

Once these steps have been completed, PIVET's Surrogacy Coordinator will collate the required documentation for consideration by PIVET's Medical Director, who will then apply to the RTC for approval to proceed with the Surrogacy arrangement.

Creating the Embryos

Once RTC approval has been received, the process to generate the embryos can proceed. This process is the same as for IVF patients and information sheets are available. In the instance that the Arranged Parent(s) have embryos from previous IVF attempts, approval must still be attained to utilise those embryos in a Surrogacy arrangement. The Act does not allow for the creation of embryos, specifically for a Surrogacy arrangement, before written approval of the arrangement by the RTC. However, it may be possible to collect and freeze your oocytes before the final RTC approval. These oocytes will still require a 180 day quarantine period and may allow creation and transfer of embryos as soon as approval has been given.



Cryostorage before transfer

Once the embryos have been created, they will be cryopreserved by a process known as Vitrification. A quarantine period of 180 days must be completed prior to embryo transfer. The reason for the quarantine period, is to complete screening tests for you and your partner, for infectious diseases which may take this time frame to be revealed. Once quarantine is completed, the Birth Mother will be contacted and following medical review, will be placed on a hormone regimen that will synchronise the best time to transfer the embryo.

In line with current PIVET practice, it is strongly recommended that only single embryo transfers occur. Even with one embryo, there is always the possibility of a multiple pregnancy and this outcome is one issue that needs to be discussed during the initial Surrogacy arrangements. More than one transfer may be required for a pregnancy to eventuate. It is important to note that, as with all IVF procedures, pregnancy does not always occur and your expectations should be realistic. About one pregnancy results from every three embryo transfers and this largely is governed by the age of the Arranged Mother / Donor at time of egg collection.

Traditional Surrogacy

If you are planning Traditional Surrogacy, your partner will need to have sperm frozen and quarantined for 6 months. Once approval has been granted to proceed by the RTC, your Birth Mother will need to be monitored for insemination at ovulation or set up to proceed to IVF.

After the birth of the child

You will need to seek independent advice from your legal representative but in summary, it is PIVET's understanding that:

- You may assume responsibility for the baby shortly after the delivery but the Birth Mother and her partner are named on the Birth Certificate until the Parentage Order is made. After 28 days, you may apply for a Parentage Order where the legal responsibility for the baby passes from the Birth Mother (and her partner) to you and your partner. A new Birth Certificate is issued.
- The Family Court has full responsibility for this legal transfer.



6. INFORMATION FOR THE BIRTH MOTHER

How do I become a Surrogate?

You will either be approached by, or you may offer to do this for a family member or friend. Together with your potential Arranged Parent(s) an appointment should be made with one of PIVET's Fertility Specialist to obtain more information. Counselling is always available even at these preliminary stages of your enquiry. If you are interested in Surrogacy as a genuine altruistic gift, then you may contact PIVET Medical Centre and speak to our Surrogacy Coordinator. While the Act restricts PIVET from actively recruiting potential Surrogates (Birth Mother's), we are able to facilitate contact between you and the potential *Arranged Parent(s)*.

If after the preliminary discussion you remain interested, then you (and if applicable, your partner) will need to follow the same process described above for the Arranged Parent(s). The key aspects of the medical consultations will be your health and well being, your potential to conceive and subsequent ability to carry a pregnancy. The RTC will consider your suitability based on these factors and upon reaching 25 years of age and having already given birth to a live child, (Section 17). The counselling consultations will explore and ensure that you understand the processes, the risks and the possible complications that may arise. When the process is followed the intended outcome will be the transfer of parentage of the child to the arranged parents by the Family Court.

A key aspect of the initial process is the legal arrangements between the Arranged Parent(s) and yourself (and if applicable, your partner). This may include discussing and agreeing on such issues as multiple pregnancy, potential risks and complications to the child, your health and lifestyle management during the pregnancy and reimbursement of any potential monetary losses within the guidelines of the Act (it is important to remember, that all Surrogacy in WA is altruistic).

Any additional financial rewards outside those allowable are illegal and both you and the Arranged Parent(s) are liable for prosecution if any undisclosed arrangements are carried out.

After the approval to proceed with a Surrogacy Arrangement from the RTC

Once the RTC approval has been granted, the embryos generated and quarantine period completed, the Surrogacy Coordinator will contact you and arrange an appointment for you to see a Fertility Specialist who will organise a treatment management plan to synchronise the best time to transfer the embryo.

About one in three women fall pregnant after an embryo transfer so you need to be realistic about the likelihood of becoming pregnant. You may need to try several times before either a pregnancy occurs or all the embryos are used. PIVET understands the emotional strain you may be experiencing therefore we strongly encourage the support of our counsellor.

Under 'Direction 12 and 13', each party to a surrogacy arrangement should have access to counselling and support services at each of the following times:

- i. Following a decision by the Council in relation to an application for the approval of a surrogacy arrangement.
- ii. During treatment in connection with a Surrogacy arrangement.
- iii. Following a decision to discontinue treatment.
- iv. Following miscarriage or birth of any child born in connection with a surrogacy arrangement.

If a pregnancy results, reasonable efforts need to be made to facilitate counselling between the birth mother and arranged parents at each of the following times:

- i. 20 weeks after the beginning of a pregnancy.
- ii. 34 weeks after the beginning of a pregnancy.
- iii. Within 14 days after a miscarriage or the birth of a child.



After the birth of the child

If you fall pregnant and deliver a baby, that the Arranged Parent(s) have access to the baby from birth. Legal transfer of responsibility via a Parentage Order is made by *The Family Court*. This may be sought 28 days after the baby is born but prior to 6 months from the day of birth.

You will need to seek independent legal advice and together with the approved parents agree on an "approved plan", which deals with matters relating to the child and balances the rights and responsibilities of all parties involved in the arrangement.

7. WHERE DO I START

Please contact PIVET's Surrogacy Coordinator who can assist you with any enquires and provide you with information sheets on related procedures / processes.

8. BIRTH CERTIFICATES

- **First Birth Certificate**
By current law, the woman who carries the pregnancy and delivers the baby is the legal mother. By law her husband or partner is the father of the child. Therefore, the first Birth Certificate is issued in the name of the *Birth Mother* and her husband / partner.
- **Second Birth Certificate**
After the Parentage Order is made a second Birth Certificate can be issued showing the Arranged Parent(s) as the mother and father of the child. This is the Birth Certificate intended for general use e.g. for the child to gain school enrolment, passport, drivers licence etc. This Birth Certificate is dependent on the Parentage Order being made.



*The above information is intended as a guide only.
The actual processes and formalities will be tailored for individual circumstances.*

9. FURTHER READING

- PIVET Medical Centre: www.pivet.com.au
- Government of Western Australia, Department of Health: www.health.wa.gov.au
- Online Legislation and Legislative Information Databases: www.slp.wa.gov.au
- Reproductive Technology Council: www rtc.org.au
 - *Human Reproductive Technology Act 1991*
 - *Artificial Conception Act 2008*
 - *Surrogacy Act 2008*
- Family Court of Western Australia: www.familycourt.wa.gov.au/S/surrogacy.aspx

10. SURROGACY APPLICATION CHECKLIST

- Medical Practitioner Report.
- Gynaecologist Report.
- Suitability and Obstetric History of Surrogate.
- Completed and Signed Surrogacy Arrangement.
- Counselling Report.
- Independent Clinical Psychologist Assessment Report.
- Legal Advice obtained and detailed regarding independent advice provided to the parties documented.
- Surrogacy Application Forms.



RISKS, SIDE EFFECTS AND OTHER CONSEQUENCES OF ASSISTED REPRODUCTIVE TECHNOLOGY

1. RISK, SIDE EFFECTS AND OTHER CONSEQUENCES

Assisted reproductive technologies and related procedures such as Ovulation Induction(OI), Intrauterine insemination(IUI), In vitro fertilisation (IVF), Intracytoplasmic sperm injection (ICSI) and Frozen Embryo Transfer (FET) may include some risks, side effects and other consequences. In addition to the risks involved with any operative procedure, such as those associated with a general anaesthetic, the possible risks and side effects of IVF and comparable procedures include the following:

1. Ovulation inducing drugs may cause development of benign (non-cancerous) cysts, hyperstimulation, multiple pregnancy (leading to an increased risk of miscarriage or premature labour) weight gain, temporary hot flushes and/or minor eye disorders.
2. During an IVF cycle, the FSH injections cause high levels of oestrogen, resulting in copious amounts of the "egg white" mucus that you may associate with impending ovulation. **Don't worry - your *Lucrin, Synarel, Orgalutran or Cetrotide* will prevent ovulation from happening prematurely.**
3. The use of *Lucrin*, one of the drugs prescribed for ovulation induction, has not yet been approved for use for this purpose. However the drug has been in use worldwide for some time and studies performed both in Australia and around the world indicate improvement in pregnancy rates with the use of this drug.
4. The taking of blood samples may cause discomfort and/or development of a bruise at the needle puncture site.
5. Ultrasound-guided egg retrieval may cause discomfort during or after the procedure and can occasionally cause bleeding or puncture of abdominal organs or infection.
6. Laparoscopy may cause discomfort after the procedure. It may also be occasionally be associated with bleeding or puncture of other organs and also infection.
7. Attempted egg retrieval using either laparoscopy or ultrasound may occasionally cause scar tissue around the ovaries.
8. Transferring the embryo to the uterus may cause discomfort and carries a small risk of infection. Slight blood spotting may be observed after embryo transfer. The transfer catheter may cause the rupture of small blood vessels in the cervix resulting in small blood spots. **Don't worry.** The embryo is in the uterus and will not be affected by this problem.
9. Emotional distress may occur as a result of the intensity of the IVF treatment cycles or the lack of success in achieving a pregnancy. Feelings of anxiety and stress may occur with circumstances such as failed fertilisation, failed collection, awaiting final results and/or anticipation of achieving a successful outcome. The treatment pressures of attending appointments may also affect work and family commitments. Due to these factors, counselling is available to PIVET patients. Please enquire with nursing staff or the front desk. The cost of one counselling session with an Approved Counsellor is included for each IVF cycle begun (*Human Reproductive Technology Act 1991, Directions 5.3*).
10. Multiple pregnancy (i.e. twins and triplets) occurs in around 3.6% (NPSU Data 2012) of conceptions resulting from IVF and related procedures because of the practice of transferring more than one embryo. This is influenced by the number of embryos transferred and your age.

PIVET Risk Model for Pregnancies (IUI & O/I)

Chance of Pregnancy		IF PREGNANT – Chance of Multiple Pregnancy				
Follicles ≥ 10mm	Pregnancy Rate	Single	Twin	Triplets	Quads	> Quads
1	0.1175	0.9550	0.0450	Occasional	0.0000	0.0000
2	0.2220	0.9000	0.0900	0.0090	0.0010	Occasional
3	0.3160	0.8400	0.1400	0.0150	0.0050	Occasional
4	0.3990	0.7900	0.1800	0.0250	0.0040	0.0010

There are certain risks that may be associated with a multiple pregnancy. Risks for the baby include:

- Preterm delivery**
 Approximately 7% of singletons, 50% of twins and virtually all triplets and higher multiples are delivered before 37 weeks of gestation. The rate of delivery before 33 weeks gestation is 1.3% in singletons and 7% in twins and 33% in triplets.
- Low Birth Weight**
 Weight at birth depends on gestational age at delivery and growth rate. Multiples tend to have a low birth weight primarily because they are often delivered preterm. However, they also grow more slowly, especially in the latter part of pregnancy, due to the limits to the maternal supply of nutrients and space within the uterus. Approximately 2.2% of singletons and 8.8% of twins have birth weights under 1500 grams.

Preterm birth and low birth weight are associated with increased risks of death and neurological impairment. Hence these babies are more likely to be admitted to a high-risk nursery.
- Perinatal Death**
 Perinatal mortality, which includes stillbirths and deaths before the twenty-eighth day of life, is more frequent in infants from multiple births than in singletons. In WA from 1990 - 2000, 1.2% of singletons, 4.7% of twins, 11.6% of triplets and 17.8% of higher multiples died in the perinatal period.
- Cerebral Palsy**
 Neurological impairment is also more common in children from multiple pregnancies. The rate of cerebral palsy is approximately 2 per 1000 in singleton children (range 1-3, WA 1.6). The risk increases 4 - 5 fold in twins and 17 - 20 fold in triplets.

Most of the increased risk of early death and cerebral palsy is explained by the higher rate of preterm birth in multiples, but there is also a small increase in risk, especially in monozygotic (“identical”) twins, for infants born at term.
- Rates of perinatal death or cerebral palsy per pregnancy**
 Since each twin or triplet in a multiple pregnancy carries a separate risk, the rates of adverse outcome per multiple are considerably greater than the risks for each infant. The risk of at least one death or case of cerebral palsy per pregnancy is 1.7% for a singleton, 10% for twins and 19% for a triplet pregnancy.

There is also an increase in the risk of speech and reading problems in toddlers from multiple pregnancies.

Increased risks for the mother during a multiple pregnancy include:

- High blood pressure.
- Severe bleeding after delivery.
- Gestational diabetes.
- Premature labour.
- Higher caesarean section rates.



Possible problems for the family after delivery:

- Fatigue and sleep deprivation in the early stages after discharge from hospital.
- The financial burden in providing for two or more children.
- These considerations are particularly important in triplet or higher order pregnancies.

PIVET Medical Centre has a strict 1 embryo transfer policy for all patients undergoing their first treatment cycle.
Consideration may be given for 2 embryos (day 3 stage) if the patient is above the age of 40 and has had at least 3 failed attempts.
The Medical Director must authorise all transfers of more than one embryo.

Some researches have suggested that there may be a slight increase in certain birth defects in babies born as a result of IVF and other related procedures. These include an increase in the incidence of Beckwith-Wiedemann Syndrome (causing gigantism and a number of disorders of various organ systems) and retinoblastoma (malignant tumour of the retina). At present, the evidence about this is not totally conclusive. Data from the National Perinatal Statistics Unit indicate that major abnormalities occurred in 4.0% of births and induced abortions after IVF, 1.8% after GIFT and 4.0% after ICSI (AIHW NPSU, 2000). These rates are no different to that of the general population. Problems of multiple birth and prematurity have been detailed in point 9 of this information sheet.



Stimulation of the ovaries causes them to enlarge with multiple follicles containing the eggs. Some women may experience pain with this and, in some instances, it can lead to abdominal swelling, internal fluid disturbances and vomiting. This is known as Ovarian Hyper-Stimulation Syndrome (OHSS) and it generally occurs after ovulation or egg retrieval. If you are not pregnant, the symptoms will disappear before your next period. If you do become pregnant, the symptoms will gradually recede by the 8th week of pregnancy. At PIVET approximately 3 or 4 severe case of OHSS occur per year and sometimes hospitalisation is necessary.

Please inform the PIVET nursing staff immediately if any of the above symptoms occur. Sometimes an enlarged ovary can undergo torsion (twisting on its pedicle) causing pain and requiring surgery or laparoscopy to unravel it. At PIVET this happens approximately once every two years.

There has been some concern recently regarding the possible relationship between fertility drugs and cancer of the ovaries and breasts. For various reasons the studies which have been reported in the medical literature are generally inconclusive, and well-designed studies are needed to ascertain the risks to women and their children. It is, however, apparent that any cancer risk from the procedures is minimal, if it exists at all.

i) Fertility Drugs and Ovarian Cancer

There are a number of factors which affect a woman's risk of developing ovarian cancer. The main ones are:

- Family history. Environmental factors may be involved but are not well defined.

- Reproductive factors (e.g. oral contraceptives, pregnancy and childbirth, and breast feeding have a protective effect; infertility and the use of fertility drugs may increase the risk).

Ovarian cancer is a relatively rare disease. In Western Australia between 1986 and 1990, ovarian cancer was the 8th most frequently occurring cancer in women. The lifetime risk of developing ovarian cancer was 1 in 109 (i.e. 1 in every 109 Western Australian Women will develop ovarian cancer in her lifetime). The incidence and mortality of ovarian cancer did not change significantly between the years 1982 and 1990, and this is consistent with Australia-wide trends (Adams et al, 1993). Research is continuing.

ii) **Fertility Drugs and Breast Cancer**

Breast cancer is the most common cancer in Western Australia. The lifetime risk of developing the disease for an Australian woman is 1 in 14. The incidence increases with age. The main risk factors for developing breast cancer are:

- Family history of breast cancer (first degree relative).
- Past history of cancer (previous breast cancer or cancer of the endometrium, ovary or large bowel).
- Reproductive factors (including early menarche and late menopause, childlessness and first full-term pregnancy after 25 years age).
- Diet and body size (fat in the diet and obesity).



- There is no evidence to date that fertility drugs increase the incidence of breast cancer. However, because of the fact that 1 in 14 Australian women will develop breast cancer in their lifetime, there is a chance that some of these women will have been treated with fertility drugs. Yet there is no conclusive evidence which proves that such treatment is associated with a higher rate of breast cancer than that which occurs in the general population. Further studies are needed to either prove or disprove any links.

iii) **Side effects of ART drugs**

• **Tamoxifen**

Tamoxifen is an anti-oestrogen and it is generally considered to increase fertility rates by inducing ovulation. Tamoxifen does not increase follicular phase FSH and LH levels, although there is an increase in oestradiol levels and luteal phase progesterone. It has, therefore, been postulated that Tamoxifen improves follicular development by direct action on the ovary rather than through the hypothalamic-pituitary axis. Usual dosage is 20mg twice daily between days 2 - 10 of a treatment cycle.

Tamoxifen should not be recommended to women with a personal or family history of blood clots, or to women who are known to have genetic defects that predispose them to thrombophilia to reduce the risk of developing blood clots with its serious consequences.

• **Growth Hormone (Saizen and SciTropin)**

It is known that certain factors called growth factors are responsible for the immediate control of the growth of follicles (fluid filled sacs containing eggs). Growth hormone in some cases increases the production of these growth factors and makes the cells within the follicle more sensitive to ovarian stimulating drugs. Due to these positive effects of growth hormone we have included it in our stimulation regimen for treating patients who have shown poor response in their previous treatment attempts.

Side effects:

Headache, visual problems, nausea and/or vomiting, hypothyroidism.

• **Dehydroepiandrosterone (DHEA)**

DHEA is used to increase growth factors to improve egg quality in preparation for your IVF cycle. DHEA, is a steroid hormone, a chemical cousin of testosterone and oestrogen. Naturally, it is made from cholesterol by

the adrenal glands, which sit atop each kidney. DHEA is chemically similar to both testosterone and oestrogen and is easily converted into those hormones. DHEA production declines in production with age in both men and women and patients (female) may require supplementation during fertility treatment.

At the low dose the consultants have prescribe, several positive effects may occur: increased libido, improved skin and hair hydration and increased energy. In a small percentage of people, mild unwanted effects like acne, nausea or fluid retention may develop. These are transient and generally resolve spontaneously on completion of treatment.

- **Recombinant FSH (Puregon, Gonal-F, Elonva, Menopur & Bemfola)**

These drugs are used to stimulate production of eggs in women and sperm in men. Recombinant FSH is manufactured synthetically by recombinant DNA technology. Both these compounds are administered daily as a subcutaneous injection. They come as a ready-made solution to be used in a pen device (either separate vial to be loaded into a pen, or a preloaded pen). These **FSH** injections may be used (ii) in higher doses for women undergoing IVF as they act directly on the ovary to stimulate multiple egg growth or ii) in lower doses for stimulation in OI or IUI cycles or FET/Low Dose Stimulation cycles. Treatment is usually started on day 3 of your treatment cycle and the dosage is adjusted according to response of the ovaries. Frequent monitoring of cycles by ultrasound and measuring hormone levels is usual due to the risk of over-stimulation.

Do not take Nurofen or similar non steroidal anti inflammatory medication (Voltaren, Naprosyn) when on recombinant FSH (rFSH) as Nurofen has been reported to decrease (rFSH) activity.

Side Effects:

Headaches, tiredness and lethargy, irritability and tearfulness, breast tenderness, nausea, enlarged tender ovaries, abdominal distention and discomfort, fluid retention, ovarian hyperstimulation syndrome (see OHSS information sheet).

- **hCG (Ovidrel or Pregnyl)**

This drug is used to mature the eggs and trigger ovulation during an IVF cycle. The drug is manufactured in a pre-prepared, single dose syringe. You may be required to inject up to three syringes for a trigger.

Side Effects:

Breast enlargement, ovarian tenderness, abdominal distention – bloating, nausea and constipation, pain at the injection site, OHSS.

- **Agonists (Synarel / Decapeptyl)**

Are drugs used to overstimulate the pituitary to the extent that FSH and LH secretion is completely suppressed. These drugs are used during IVF treatment to prevent an LH surge, which would result in an unplanned ovulation. When used in combination with injected gonadotrophins this allows for more reliable timing of the egg collection and usually an increased number of eggs being available at time of collection.

Synarel is a nasal spray used twice daily and Decapeptyl an injection daily.

Agonists can also be used to suppress conditions that may be hormonally controlled such as uterine fibroids and endometriosis,

Side Effects:

Headache, local irritation inside the nose or at the injection site, occasional hot flushes and breast tenderness, muscle weakness and pains, and double vision, 1 in 500 women have a slight allergic reaction – shortness of breath, chest pains and rashes.

- **GnRH Antagonists (Orgalutran or Cetrotide)**

In contrast to the GnRH agonists these compounds block the receptors on the pituitary to prevent the release of gonadotrophins. This results in a rapid, profound and rapidly reversible suppression of the

ovaries. This is done to prevent unplanned ovulation during IVF treatment. When used in combination with injected gonadotrophins this allows for more reliable timing of the egg collection and usually an increased number of eggs being available at time of collection.

These agents are administered daily as a subcutaneous injection, and come as a solution in a pre-filled syringe (Orgalutran) or as a powder and solution that is mixed immediately prior to administration (Cetrotide).

Relatively free of side effects.

- **Medroxyprogesterone (Provera)**

Medroxyprogesterone is used to prevent pregnancy by inhibiting ovulation. This occurs by causing the cervical mucous to thicken, making it harder for sperm to move toward the uterus and once ceased, induces menstruation. Medroxyprogesterone is used to treat amenorrhoea (the absence of menstrual periods), dysmenorrhoea (painful menstruation), and abnormal bleeding from the uterus.

Medroxyprogesterone tablets may be prescribed (i) twice daily for five to ten days, or (ii) once a day every day of the month.

Provera can also be prescribed as a pregnancy support drug (see 67.3 *Pregnancy Support Information sheet for further details on Provera in pregnancy*).

- **Progesterone or Combined Oestradiol / Progesterone Pessaries**

Provide hormonal support in the luteal phase of a treatment cycle and to increase progesterone levels in pregnancy. When commenced they must continue until the tenth week of pregnancy or a negative pregnancy test.

Progynova (Oestradiol)

Oestrogen support in the luteal phase, is usually prescribed for FET/HRT cycles, commencing on day one of the cycle and continuing until the tenth week of pregnancy or until a negative pregnancy test. The following medicines may potentially reduce the blood levels and effect of this medicine:

- *Rifamycins such as rifabutin and rifampicin*
- *Protease inhibitors such as ritonavir and nelfinavir*
- *Antiepileptic medicines such as carbamazepine, phenytoin, phenobarbital and primidone*
- *Barbiturates such as amobarbital (amylobarbitone)*
- *The herbal remedy St John's wort (Hypericum)*

Please inform the consultant if you are currently taking any of the above medications **PRIOR** to commencing Progynova.

2. COUNSELLING

Being on an IVF Program can be very stressful and it is important that you are aware of the demands it will place on you both. The medical, scientific & nursing staff, and our Counsellor will assist and support you.

3. MONITORING AND REVIEW

During and following your treatment cycle the PIVET team will monitor your progress at regular intervals. At the review stage we will make any adjustments that are necessary to ensure that you are continuing to receive the best possible care. The program will involve a lot of traveling, visits, waiting and some time in our day procedure facility or occasionally in hospital. There is also a degree of uncertainty, anxiety and emotional strain. Although this may be a natural reaction to IVF treatment and the importance of what is at stake, we feel the close relationship you will develop with the Fertility team members will help. If at any time

during the treatment cycle you have any questions, please ask and we will try to explain anything we can. We wish you every success in the IVF program and will do everything possible to help you achieve this.

4. SUPPORT WEBSITES & RESOURCES

- Reproductive Technology Council www.rtc.org.au
- Donor Conception Support Group: www.dcs.org.au
- Merck Fertility Online Portal <http://merckserono.fertilityportal.com.au>
- MSD Fertility Treatment App *iTunes & Android phones*
- Ferring Reproductive Health & Fertility Plan App www.ferring.com.au/reproductive-health



ADDITIONAL INFORMATION

1. Confidential Data Registers

As of April 1993, PIVET is required by the *Human Reproductive Technology Act (1991)* to maintain records and report to the WA Department of Health, the following information for people undergoing assisted reproductive technology:

- Identifying and non-identifying information.
- Demographic data.
- Previous treatment for infertility and treatment cycles.
- Cause of infertility (male or female factors); the use of donor eggs, sperm or embryos.
- Their storage and preparation; outcome of treatment cycle and/or pregnancy.

The information is **confidential** and identifying data will be kept separately to non-identifying data.



Under the *Human Reproductive Technology Act (1991), Amendment 1, December 2004*, any child born as a result of egg / sperm or embryo donation on reaching the age of 16 years will have access to identifying information about the donor, following approved counselling. This process may be facilitated by the Reproductive Technology Unit and clinics.

For children under the age of 16 years each donor and recipient needs to consent to sharing identifying information and the parent needs to consent on behalf of the child. There must be approved counselling of all parties (which may include the child).

All parties involved in donor conception (donors, parents of donor conceived children and donor conceived children over the age of 18 years), can register on the Voluntary Register where they may be able to access identifying information.

This depends on whether the other parties are also registered and their instructions on information to be made available. The Voluntary Register website is: www.voluntaryregister.health.wa.gov.au.

Data registers will be discussed at length with you by the staff at PIVET.

2. HRT Act (1991) Section 23

It is important to understand that under the *Human Reproductive Technology Act (1991) Section 23*, IVF can only be carried out when the person or couple are infertile or where a child would otherwise be likely to be affected by a genetic disease or abnormality.

The reason for infertility must not be age related. The health and interests of the parents and any child likely to be born will be considered when determining if treatment should be carried out.

There is now extensive information available about all aspects of infertility and assisted conception.

Please don't hesitate to ask any of the staff for further information and for reading material that you can get for yourself.

FEES AND COSTS

A current fee sheet is available from the reception staff.

Following consultation for treatment and prior to commencement of a treatment cycle, your costs will be discussed with you by a member of the administrative staff.

You will be required to sign a [Financial Consent Form](#).

Treatment costs are sometimes confusing.

As well, there may be costs associated with procedures which are billed from external medical providers.

These include:

- Anaesthetists fees
- Pathology fees
- Cytogenetic fees
- Ultrasound fees
- Certain drugs which are not covered by Medicare



QUESTIONS AND COMPLAINTS

Please feel free to discuss any concerns, questions and/or complaints relating to the handling of your personal and health information, by writing to either:

Nurse Manager

PIVET Medical Centre / Perth Day Surgery Centre
166 - 169 Cambridge Street, Leederville, Perth WA 6007
Email: info@pivet.com.au

Reproductive Technology Council

www.rtc.org.au

Health and Disability Service Complaints Office

Ph: 08 6551 7620
Country Free: 1800 813 583
Email: mail@hadsco.wa.gov.au

GLOSSARY OF TERMS COMMONLY USED IN IVF

ADHESIONS	Scar tissue from infection, endometriosis, surgery or bleeding which can distort or cause dysfunction of organs.
AMNIOCENTESIS	The removal of a small amount of fluid using ultrasound guidance from the fetal sac to check for fetal abnormalities.
ANEUPLOIDY	The presence of extra or missing chromosomes in cells.
ASPIRATION	Gentle suction used to remove an egg from a follicle.
BIOCHEMICAL PREGNANCY	Elevated hormone levels indicate a pregnancy, but implantation and continuing development of the embryo does not occur.
BLASTOCYST	The stage of a day 5 to 6 day old embryo.
BLIGHTED OVUM	A fertilised egg which does not continue to develop at an early stage.
CERVIX	A ring of muscle at the base of the uterus, extending into the vagina.
CHORIONIC VILLUS BIOPSY	The removal of a small amount of tissue from the placenta (the structure which joins the mother to the fetus) to check for fetal abnormalities.
CRYOPRESERVATION	Preservation by freezing and storage of gametes, embryos or other tissue
ECTOPIC PREGNANCY	Implantation of the embryo other than in the uterus (usually in the fallopian tube).
EGG	The female cell developed in the ovary which forms an embryo when fertilised by a sperm; also called ovum (plural ova) or oocyte.
EJACULATION	Action whereby semen containing sperm is discharged from the penis associated with male orgasm.

EMBRYO	The fertilised egg which has begun cell division.
EMBRYO TRANSFER	Placing the embryo, developed in vitro, into the uterus using a catheter threaded through the cervix.
ENDOMETRIOSIS	A condition where endometrial tissue is located outside the uterus in the endometrial cavity. It responds to hormonal changes as if it were in its correct place.
ENDOMETRIUM	The lining of the uterine wall in which the embryo implants.
FALLOPIAN TUBES	The narrow tubes leading from the top of the uterus towards the ovaries.
FERTILISATION	Penetration of the egg cell by the sperm cell, which results in cell division.
FIMBRIA	Finger-like structure at the outer end of the fallopian tube, which guides the egg, released by the ovary, into the tube.
FLUSHING	Refilling a follicle with a special fluid (media) to ensure aspiration of the egg.
FSH (Follicle Stimulating Hormone)	A hormone produced by the Pituitary gland, which controls growth of the ovarian follicle and maturation of egg cells in a woman and sperm production in a man.
GAMETE	A reproductive cell (sperm and eggs).
GIFT (Gamete Intra Fallopian Transfer)	Sperm and eggs are deposited into the fallopian tubes, either through a catheter placed into the cervix or via a laparoscope into the abdominal cavity.
hCG (Human Chorionic Gonadotrophin)	A hormone produced by the developing embryo and later by the placenta. It is also administered during IVF, GIFT, TEST, PROST, IUI and Ovulation Induction to induce ovulation at a precise time (referred to as the trigger injection).
HYPER STIMULATION	An exaggerated response of the ovaries to the drugs given, resulting in bloating of the lower abdomen, pain, nausea, discomfort and enlarged ovaries with associated discomfort.
IMPLANTATION	The embedding of an embryo in the endometrium of the uterus.
INFERTILITY	The inability to become pregnant after 12 months of regular unprotected intercourse.
IVF (In Vitro Fertilisation)	The combining of a selected sample of mature sperm with mature eggs in a petri dish or test tube for fertilisation.
LAPAROSCOPY	A surgical procedure in which a laparoscope with an attached light is inserted into the abdomen, so the surgeon can perform procedures with minimal invasion using video control.
LH (Luteinising Hormone)	A hormone that is produced by the Pituitary gland and rises at ovulation, controlling the release of a mature egg from a follicle in the female, and male hormone production (testosterone) in men.
LUTEAL PHASE	The segment of the menstrual cycle, after ovulation but before menstruation
MENSTRUAL CYCLE	Recurring changes in a woman's body, during which hormonal activity causes regular development of follicles and eggs, as well as changes in the lining of the uterus. Sloughing of uterine cells manifests as bleeding

from the vagina at the end of a cycle in which pregnancy has not occurred.

OVARIES

Small organs located in the pelvic cavity, on either side of the uterus, which contains eggs.

OVULATION

The release of a mature egg cell from the ovary.

PITUITARY

A hormone producing gland located at the base of the brain.

PGD

(Pre implantation Genetic Diagnosis)

A test performed on the embryo to detect a limited range of genetic disorders.

PGS

(Pre implantation Genetic Screening)

A test performed on the embryo to detect an abnormal number of chromosomes (aneuploidy). Currently only chromosomes X, Y, 13,15,16,18,21 & 22 are able to be assessed.

SEMEN

The fluid discharged by the male on ejaculation, which contains sperm and other glandular secretions.

SCSA

(Sperm Chromatid Structure Assay)

A test to determine the level of DNA fragmentation in sperm.

TESTES

Male organs located in the scrotum, which produce sperm cells (into the semen) and the male hormone testosterone (into the bloodstream).

UTERUS

A small pear shaped organ in which the embryo implants and the fetus grows until delivery.

VAGINA

A distensible tube shaped organ leading from the cervix, which can contain the penis during intercourse and allows sperm access to the uterus and fallopian tubes and through which a baby is born.

VITRIFICATION

A rapid cryopreservation technique for eggs and embryos. Superior to slow freezing due to the absence of cell damage by crystal formation.

ZYGOTE

Fertilised egg.



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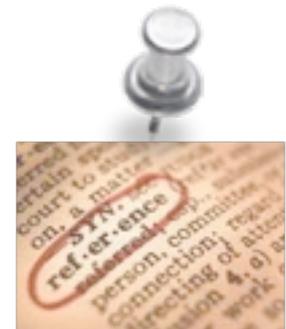
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CLINIC HOURS



CONTACT DETAILS

PIVET LEEDERVILLE - CLINIC HOURS AND CONTACT NUMBER

166 - 168 Cambridge Street, Leederville, Perth 6007, Western Australia

Clinic	Mon - Fri	7.30 am - 4:30 pm	08 9422 5400
Laboratory	Mon - Fri	7.30 am - 4:30 pm	08 9422 5400
Follicle Tracking	Mon, Wed & Fri	7.30 am - 9.30 am	08 9422 5400

After Hours Emergency Paging Service (Emergencies Only)
WADMS - 08 9321 9133

WEMBLEY PHARMACY

361 Cambridge Street, Wembley, Perth 6014, Western Australia

Hours	Mon - Sun	8 am - 10 pm	08 9387 3079
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USHER PHARMACY

26 Cranbrook Way, Bunbury 6230, Western Australia

Hours	Mon - Fri	8.30 am - 5.30 pm	08 9795 7631
	Sat	8.30am - 12.30pm	
	Sun	Closed	

MY DOCTOR



NOTES