

# Meet the Usual Suspects?



## What is endometriosis?

Endometriosis is a disease characterised by:

- Presence of functioning endometrial tissue outside the uterine cavity in so-called 'ectopic sites' such as on the ovaries, fallopian tubes, vagina, cervix, uterine and ovarian ligaments or in the Pouch of Douglas. Other sites may include bowel, ureters or bladder.
- > Inflammation of tissues as a reaction to the growth of the endometrium at these ectopic sites.

#### What happens to the endometrium in normal women?

The lining of the uterus (endometrium) has the most remarkable growth potential of any tissue in the body. Various substances, some which are made within the endometrium itself, and some of which are derived from the circulating blood, promote this growth. The most potent stimulant of endometrial growth is the female hormone called oestrogen. In women, oestrogen is normally produced in the ovary by the egg follicles, and it then circulates in the blood. The endometrial cells lining the uterus actively and preferentially absorb the oestrogen, which then stimulates the cells to grow and proliferate. As part of the normal function of the endometrium, there is no inflammatory reaction. The endometrium is normally shed during a woman's period, after the ovarian follicle has died and the oestrogen level has fallen. In nearly all women, some of the endometrium refluxes up the fallopian tubes. It spills out of the tubes, over the ovaries, and into the pelvis, which is lined with a thin layer of tissue called the peritoneum. The peritoneum normally absorbs this refluxed tissue with no inflammatory response, as with any other part of the body's natural response mechanism. Consequently, the peritoneal lining stays smooth so that the tubes and intestines can function normally.

#### What happens to the endometrium in women who have endometriosis?

Women who have endometriosis may have a relatively higher level and longer duration of exposure to oestrogen, or may have higher oestrogen receptor sensitivity. These relatively high levels of oestrogen might also be capable of stimulating a thicker endometrium and more substantial pelvic contamination because of increased menstrual volume and higher incidence of retrograde bleeding.

- The endometrium is more vascular;
- More of the endometrial tissue that is shed stays alive, or vital;
- More of the sloughed tissue refluxes up the fallopian tubes, bathing the peritoneum and pelvic organs in more endometrial reflux that is also more vital.

Whether the refluxed endometrium itself grows, or whether it stimulates the tissues in the pelvis to grow endometrium, is uncertain. In any event, there is growth of endometrium in these tissues outside the uterus.



Women who have endometriosis also have an abnormal autoimmune response, because the body's immune response to the initial spill and growth of the refluxed endometrium is not simply by absorption, but by an inflammatory reaction.

#### **Endometriosis and fertility**

Endometriosis is a significant cause of infertility, because in 10% of couples that have difficulty conceiving the woman partner is diagnosed with mild endometriosis.

#### Why do women who have endometriosis have more difficulty conceiving?

Women who have endometriosis have more difficulty conceiving for a number of reasons, including:

- The endometrium may be less responsive for implantation. Inflammation within the uterus, may cause slight bleeding, this blood oxidises (rusts!), releasing chemicals that inhibit the development of the hatching embryo.
- Sexual intercourse may occur less frequently because of pain from inflamed growths on pelvic ligaments.
- Fallopian tubes or ovaries may be scarred as a result of inflammation.
- Inflamed pelvic tissues may digest sperm.
- It may be physically impossible for the tube to pick up the egg because of a large cyst within the ovary. These cysts can develop from ectopic endometrium on the surface of the ovary.
- Ovarian follicles may not develop, rupture and release the eggs well because inflammation in and around the ovaries may interfere with this important function.

### What are the symptoms of endometriosis?

In a woman presenting with infertility, endometriosis may be suspected if the woman experiences pain or severe discomfort around the time of her period, ovulation, or during sexual intercourse. She may also experience irritable bowel symptoms if the endometriosis involves the bowel. In less common cases, endometriosis is completely silent and the woman experiences no symptoms. Although endometriosis may also be suspected because of tenderness on examination, an ovarian cyst, or abnormal fluid collections seen during an ultrasound scan, endometriosis can only be diagnosed by the presence of characteristic flared, haemorrhagic or scarred lesions (like a burn) during a laparoscopy. This procedure needs to be done under general anaesthetic.

#### **Causal Factors of endometriosis**

The cause of endometriosis is unknown, although we can begin to understand the growth of the Endometrium by understanding the function of normally sited endometrium. There is also a genetic component to endometriosis.

## What are the medical treatments for endometriosis?

For rational treatment of endometriosis, the major triggers to the development of endometriosis need to be addressed. These are:

- A genetic effect of growing more vital hypervascular endometrium; and
- An inherent ability to develop an inflammatory over-reaction to the abnormal endometrial stimulus.

This means that the treatment of endometriosis needs to:

- Restrict the ability of the endometrium to grow; and
- Ensure the immune system is not stressed.



Unfortunately, our understanding of the immune system and the inflammatory over-reaction is primitive, making it difficult to treat. As endometriosis is usually diagnosed at laparoscopy, it is often convenient to destroy or remove the inflamed tissue growths or scars at the time. However, other 'seeds' endometrium may grow so any benefits may be short-lived. Fortunately, some women's bodies heal themselves of endometriosis. Medical treatments such as progestogens, which block follicle development and thereby inhibit growth of the endometrium, are reasonably effective in controlling pain and reducing cyst formation. However, medical treatments also block the body's ability to conceive, so women who wish to conceive only use them to settle inflammation prior to specific fertility treatments.

#### What fertility treatments can assist women who have endometriosis?

- Lipiodol (poppy seed oil) endometrial bathing / tubal flushing
- Intra-uterine insemination with mild hyperstimulation using fertility drugs
- In-Vitro fertilisation

Laparoscopic surgical removal of endometriosis has been shown to improve fertility, as well as helping to resolve pain symptoms.

• Alternative treatments – such as herbs – may have an effect, although this is not scientifically proven

#### Is medicine likely to find better treatments for endometriosis?

The immune system has the ability to heal itself, so the inflammation associated with endometriosis can be overcome. But there is no treatment yet that will heal over-active immune systems. Nor is there any genetic treatment that will make the endometrium behave more normally. Hopefully medicine will soon be able to identify the exact problems within the genetic and immune systems that occur in women who have endometriosis.

Contributed by Dr Neil Johnson, Fertility Plus

#### Self help

Age is a factor for women with endometriosis, as is time that you have been trying to conceive. If circumstances allow, start trying for a family by age 30.

#### Alternative therapies

Naturopathy, medical herbalism, nutrition and acupuncture are all modalities that can help support and guide women who have endometriosis.

#### The naturopathic approach to endometriosis

Estrogen and progesterone work in synchronisation with each other to achieve hormonal harmony. In women with endometriosis there is a relative dominance of estrogen that contributes to the growth and inflammation of the endometrial implants. Certain lifestyle choices and conditions can contribute to this estrogen dominance syndrome, especially a low- fibre diet, overloading the liver with internal toxins and absorbing toxins from the environment (referred to as xenoestrogens or endocrine disruptors).

#### • High Fibre Diet

A low-fiber diet causes estrogen levels to be higher, while a diet high in fiber results in decreased estrogen levels in the bloodstream. Why? Excess estrogen is excreted in the bowel. When stool remains in the bowel for a longer time, as in constipation, the estrogen is reabsorbed. Studies have shown that women on a high fiber diet have lower levels of circulating estrogen.

#### Overloading the Liver



The liver detoxifies our body, protecting us from the harmful effects of chemicals, elements in food, environmental toxins, and even natural products of our metabolism, including excess estrogen. Anything that impairs liver function or ties up the detoxifying function will result in excess estrogen levels, whether it has a physical basis, as in liver disease, or an external cause, as with exposure to environmental toxins, drugs, or dietary substances. Estrogen is produced not only internally but also produced in reaction to chemicals and other substances in our food. When it is not broken down adequately, higher levels of estrogen build up. The estrogen dominance syndrome can be evoked in women by too much alcohol, drugs, or environmental toxins, all of which limit the liver's capacity to cleanse the blood of estrogen.

#### • Environment

We live in an estrogenic or feminising environment. "Xenoestrogens", such as PCBs, phthalates, pesticides and DDT, cause estrogenic effects. Chlorine and hormone residues in meats and dairy products can also have estrogenic effects.

• Healthy Hormone Foods (choose at least one from each group daily)

Herbs and Spices - ginger, rosemary, turmeric, dill fennel, parsley

Nuts and Seeds - pumpkin seeds, sesame seeds, sunflower seeds, almonds, cashews, brazil nuts

Grains and Legumes - chickpeas, quinoa, millet, bulgur, buckwheat, brown rice

Fruits - blueberries, strawberries, oranges, grapes, avocados, bananas, figs, blackberries

Meat, poultry, fish, dairy - yoghurt and deep sea fish

*Vegetables* - broccoli, cauliflower, brussel sprouts, kale, spinach, cabbage, celery, onion, alfalfa sprouts

Beverages - water, green tea, dandelion tea, chamomile tea

*Lifestyle* - regular aerobic and weight bearing exercise, time out, relaxation techniques. Limit alcohol to <1 drink daily

#### Xeno-estrogens

It is beneficial to reduce the exposure to the chemicals in our environment that mimic estrogen. Below is a list of the more common forms.

**BPA** (**Bisphenol A**) – used to harden polycarbonate plastics, found in plastic containers, canned food, white fillings

**Phthalates** – plasticizers, used in the production of plastics. Found in cosmetics, perfumes, aerosols, paints, air freshners, shampoos, skin moisturizers, nail polishes, shower curtains, plastic toys, 'fragrances'

**PCBs** (*Polychlorinated biphenyls*) - fat-soluble, accumulate in our body fat and in animal fats we consume. Found in fluorescent lighting, electrical equipment, hydraulic fluids

**Parabens** – chemical additives widely used in cosmetics, pharmaceuticals and food production as preservatives, antibacterial and antifungal agents

*Volatile Solvents* – inhaled as fumes or vapours. Found in gas, exhaust, paints, polyurethanes, dry cleaning chemicals

**PFAs (perfluorinated compounds)** – these are persistent organic pollutants that make products stain, grease and water repellent. Found in paper food containers, fast food wrappers, Teflon, Scotchguard **PBDEs (polybrominated diphenyl ethers)** – flame retardants found in home and building materials, insulation, cars, furnishing, bedding, textiles e.g pyjamas

Pesticides and Insecticides - used in the home, garden and sprayed on our fruit and vegetables

#### • Resetting the Balance

1. Optimise your weight.



- 2. Limiting environmental exposure to xenoestrogens along with implementing a proper diet, exercise and supplements can help reverse the syndrome of estrogen dominance.
- 3. Exercise regularly
- 4. Eat plenty of fibre

Contributed by Loula George, Fertility NZ and Mother-Well Holistic Health

For more information on Endometriosis, see <u>www.endometriosis.org.nz</u>





## What is male factor infertility?

The World Health Organisation (WHO) standard for healthy sperm is as follows:

- Volume >1.5 ml
- Viscosity
- Sperm count >15 million / ml
- Motility (progressive) >32%
- Motility (total) >40%
- Morphology >4%

Male factor infertility will be present in 30-50% of couples, either as the single major cause of their fertility problem or as part of multi-factorial problem. Low sperm morphology (fewer than 5% of the sperm appear normal when assessed microscopically) can lead to failure of fertilisation with IUI or IVF. It can occur even with normal sperm numbers and motility.

#### **Chances of pregnancy**

Unless there is absent sperm production or an extremely low count (less than 5 million/ml) it is the circumstances of the couple's infertility such as the duration of infertility, previous pregnancy history and also female partner's age that are the most important factors in predicting future chances of conception. The results of the semen analysis therefore for each couple must be interpreted in the light of each couple's individual circumstances.

#### Symptoms and diagnosis of male infertility

Physical symptoms will only be present in a small number of male infertility cases, such as with retrograde ejaculate (where the semen is not ejaculated), or an anatomical factor is present (such as an undescended testicle). For most couples trying to conceive, a semen analysis will be recommended by either a GP or a fertility clinic, early in the investigation stage into a couple's fertility. It is often not until the results of the semen analysis are revealed that the man learns that there is an issue with his sperm. Although a semen analysis is essential for diagnosing male infertility, a detailed history should also be taken, including a sexual history, and also possible exposure to any environmental toxins.

Previous genital surgery, including for an undescended testicle, previous inguinal hernia repair or previous significant infections such as chlamydia or mumps orchitis will also be relevant.

Physical examination is important, looking at the size and consistency of the testicles, whether any abnormal swellings are noted, if there is a varicocele present and also whether the vas deferens is palpable. If there is any abnormality on the initial semen analysis, a further analysis should be undertaken at a tertiary fertility laboratory looking carefully at sperm motility and morphology (shape) and testing for antisperm antibodies. Hormone assays may be useful and should include FSH, testosterone and prolactin levels.



A blood test for Karyotyping, to check the chromosomes, may be useful to exclude certain genetic conditions. There are also newer tests that measure the integrity of sperm DNA (SCSA, Tunel, Comet) and the ability of sperm to bind to the zona (HBA).

## **Causal factors**

For at least half of sperm problems, the cause remains unknown (idiopathic) although there is an increasing understanding that genetic factors may play an important role. Ten percent of men with absent sperm production or an extremely low count (azoospermia and severe oligospermia) will have small pieces missing from their Y chromosome (microdeletions) as the cause for the abnormal sperm production. There are tests for Y micro-deletions.

Male obesity with reduced circulating testosterone levels can influence sperm quality as can heavy alcohol intake, cigarette and marijuana smoking and certain medications.

Oxidative stress-related damage to sperm caused by free radicals has been shown to be an increasingly important issue. Recent research suggests obesity can cause oxidative stress to sperm.

Blocking the free radical damage by the use of anti-oxidant preparations can be a useful management option if increased DNA damage is thought to be a contributing factor.

Regret following a vasectomy is an increasing problem and it is estimated that 10% of men will seek either reversal of vasectomy or surgical retrieval of sperm for use with micro-injection.

## **Treatment options**

Occasionally a hormonal imbalance will be discovered on testing which can be treated with replacement gonadatrophin injections to improve the sperm count. Unfortunately, cases where medication will improve the sperm count are relatively rare.

- Lifestyle changes such as losing weight if obese, reducing alcohol and cigarette intake and wearing boxers rather than tight underwear, can improve quality of sperm. Note that this may not help if there is significant abnormality present.
- Donor insemination is used much less frequently now as a treatment for male infertility, mainly because of the introduction of micro-injection. Treatment with donor sperm in an otherwise healthy woman should result in pregnancy rates of 15-20% per cycle.
- Intrauterine insemination IUI (artificial insemination using partner's sperm) is used occasionally for the treatment of male infertility but is again unlikely to be useful if a significant sperm abnormality is present. Randomised controlled trials show that intrauterine insemination is better than timed intercourse for the treatment of male infertility, particularly when used with ovarian hyperstimulation. Nevertheless, success rates of only 5-10% per cycle are reported in most studies when IUI is performed for male fertility.
- ICSI (micro-injection) involves the direct injection of the sperm into an egg as part of in vitro fertilisation (IVF) treatment. It is primarily used when a major sperm defect has been identified or where there has been poor fertilisation with ordinary IVF. It has been particularly successful when there is low sperm morphology.

There are new methods available which attempt to isolate mature, structurally-intact sperm with high DNA integrity which are then injected into the egg.

- PICSI selects a mature sperm, which could bind to the zona.
- IMSI uses high magnification to select a sperm without vacuoles.



These methods may be suggested after a failed ICSI cycle. Studies are needed to confirm that PICSI and IMSI improve outcomes over conventional ICSI.

Clinical pregnancy rates of 30-40% per cycle are usual with micro-injection so long as there is good fertilisation and the woman is aged less than 40. Long-term follow up of children born after using ICSI has been documented. The chance of congenital abnormalities may be slightly higher with ICSI than with standard IVF, and there may be slightly more children born with X or Y chromosome abnormalities. If the male infertility is caused by a micro-deletion of the Y chromosome, it is very likely that a male child will inherit the same Y micro-deletion as his father.

Contributed by Dr Greg Phillipson, Fertility Associates and Fertility NZ

## Self Help

The formation of sperm may take up to 100 days and during this time the rapidly dividing germ cells are susceptible to damage. Ideally, to ensure sperm are as healthy as they can be, it is important that conception attempts are preceded by 3 months of healthy lifestyle changes so that the sperm can develop in optimal conditions.

- Stay cool Increased scrotal temperature can hamper sperm production.
- **Don't smoke** Men who smoke cigarettes are more likely to have low sperm counts. Smoking can also decrease sperm movement and cause sperm to be misshapen.
- Limit the amount of alcohol you drink Heavy drinking can reduce the quality and quantity of sperm. Heavy consumption of alcohol affects your hormone levels, in particular your testosterone levels. It also affects the ability of your testes to mature the sperm properly. This leads to poor semen quality but the effect is reversible.
- Steer clear of illegal drugs Like cigarettes, marijuana can decrease sperm movement and cause sperm to be misshapen. Cocaine and heroin also interfere with healthy sperm. The effect of synthetic drugs such as methamphetamine ('P') is less known.
- **Caffeine** Recent reports suggest that an excessive amount of caffeine can reduce and retard the quality of sperm a man produces. As little as 3 cups of coffee a day can have a seriously detrimental effect.
- **Be cautious with medications** Calcium channel blockers, tricyclic antidepressants, anti-androgens and various other medications can contribute to fertility issues. Anabolic steroids can have the same effect. Chemotherapy drugs and radiation treatment for cancer can cause permanent infertility.
- Manage stress Stress can decrease sexual function and interfere with the hormones needed to produce sperm.
- Ageing Sperm motility and the number of healthy sperm might decline after age 50, affecting a man's fertility. Some research suggests that women who become pregnant by older men have a slightly higher risk of miscarriage. A father's increasing age has also been associated with a higher risk of both autism and schizophrenia in children.
- **Frequency of sex** Frequent ejaculation is better for the health of sperm while trying to conceive. One day's abstinence gives better quality sperm. Periods of abstinence longer than three days can be detrimental because of the accumulation of aged sperm. These are also the guidelines given when producing a sperm sample to be tested.



- **Exercise** Regular moderate exercise (25-30mins at least 5 days per week) can benefit overall physical, emotional and general wellbeing which has a positive effect on fertility. Excessive exercise (more than 8 hours per week) can negatively affect fertility in both men and women.
- Maintain a healthy weight Some research suggests that obesity negatively affects sperm quality, reducing both sperm count and sperm movement. It can also cause decreased libido and erectile dysfunction.
- **Nutrition** Eating a healthy fertility diet in the 3 months preceding conception attempts can help protect and encourage healthy DNA, promote sperm health and encourage and support a healthy libido.

#### **Important Nutrients for Male Fertility**

**Zinc** - Having a zinc deficiency can reduce testosterone levels. Zinc has been shown to raise testosterone and increase fertility. Zinc deficiencies are very common in both men and women due to our soils being low in this nutrient and also zinc can be damaged when foods are cooked or processed. Foods rich in zinc are beef, lamb, oysters, shrimp, venison, sesame seeds, pumpkin seeds and green peas.

Folic acid - Men with low levels of folate had increased risk of chromosomally abnormal sperm, which could result in birth defects such as Down's syndrome, or an increase in miscarriage. Folic acid is found in lentil beans (1 cup provides almost your entire daily needs), pinto beans, garbanzo beans, asparagus, spinach, black beans, navy beans, kidney beans and collard greens. One serving a day of any of these foods provides anywhere from 50-90% of your daily needs.

**B12** - Has been shown to increase sperm counts. Many people are deficient in B12; meat eaters and vegetarians alike. Some foods rich in B12 are dairy and animal products. For most people, healthy levels of B12 depend on healthy digestion, which most people lack due to eating a highly processed diet. Foods high in B12 are chicken liver, sardines, mussels, oysters, eggs, beef and lamb.

**Vitamin C** - Protects sperm from oxidative damage. It will help to increase the quality of sperm in smokers and rescues sperm agglutination (when they clump together). Vitamin C is another nutrient that is sensitive to cooking and processing, so it important to get it from eating foods raw. Some foods that are rich in vitamin C (and should be eaten raw) are **kiwifruit**, **papaya**, **bell peppers**, **broccoli**, **brussels sprouts**, **strawberries**, **oranges**,, **cauliflower and kale**.

L-Carnitine - This amino acid is a necessary nutrient for sperm cells to function normally. Studies show that supplementing with L-Carnitine helps to normalize sperm motility in men with low sperm quality. Foods rich in L Carnitine are nuts, seeds, and many vegetables, including artichokes, asparagus, beet greens, broccoli, brussels sprouts, collard greens, garlic, mustard greens, okra, and parsley.

**CoQ10** - Acts as an antioxidant protecting the sperm cells from damage. Studies have shown a connection between CoQ10 levels and sperm health. CoQ10 has also been shown to increase sperm motility. It has been shown that our CoQ10 levels decrease as we age. Foods rich in CoQ10 are **beef**, marinated herring, rainbow trout, salmon, organ meats, peanuts, pistachios, sesame seeds, raw broccoli, strawberries, oranges, eggs, plus whole grains that still contain the germ.



**Betacarotene/Lycopene** - Has been shown to improve both sperm concentration and motility. Food sources are **fish liver oils, egg yolk, carrots, tomatoes, rock melon, pumpkin, kumara and spinach.** 

**Selenium** - is a very important nutrient for all parameters of sperm health. It is also necessary for mitochondrial protection and function. Unfortunately, it is also a nutrient that is low in our soils. Food sources include **brazil nuts, mushrooms, egg yolks, wholemeal flour, oats, fish and sesame seeds.** 

**Essential Fatty Acids** - Lowered levels of essential fatty acids have been demonstrated in infertile men. It is very important for the formation of sperm. Food sources include fish, fish oils, flaxseed oil and walnuts.

#### **General Dietary Guidelines**

- Eat plenty of antioxidant rich foods, including vegetables and fruit
- Ensure adequate protein fish, chicken, lean red meat, eggs, dairy, legumes
- Reduce saturated fats and trans fats
- Ensure sources of healthy fats olive oil and other vege oils, nuts, seeds, avocados
- Reduce sugars and refined carbohydrates , ensure adequate amounts of whole grains
- Avoid processed foods which are often high in fat, sugar and/or salt
- Eat organic where possible
- Drink plenty of fresh water
- Limit caffeinated beverages such as coffee, tea, caffeinated soft drinks, energy drinks
- Avoid or reduce alcohol consumption

#### **Environmental Toxicity and Sperm Health**

Hidden environmental toxins and hormone disruptions (xenoestrogens) are the most probable culprits for the reduction in sperm numbers and quality over the last 50 years. They are found all around us in a variety of unsuspecting places, such as cleaning products in the home, plastic food packaging, and personal care products that we use on a daily basis. Many men also work with and around toxic substances, chemicals and heavy metals, which can be damaging to sperm cells. Precautionary measures should always be taken when exposed to such substances

#### Radiation

Exposure to various kinds and amounts of radiation can ultimately affect fertility. This is due to the sensitivity of germ cells to x-rays and gamma rays. This includes laptops on laps, cell phones in pockets and electric blankets. Cell phone usage has been linked with decreases in progressive motility of sperm, sperm numbers and morphology. One study evaluating 52 men demonstrated that men who carried a cell phone around the belt line or hip region were more likely to have decreased sperm motility compared to men who carried them elsewhere or who did not carry one at all.

Contributed by Loula George, Fertility NZ and Mother-Well Holistic Health





## What is Polycystic Ovary Syndrome?

Polycystic ovaries (PCO) is the description for ovaries that contain 12 or more follicles per ovary (normally there are 1 or 2 follicles per ovary). The use of polycystic ovary is misleading; as the so-called cysts are small follicles that fail to develop - sometimes known in medical terms as atretic follicles.

Polycystic Ovarian Syndrome (PCOS), however, is a more complex condition and may be diagnosed or defined in different ways depending on which country a woman lives in. The most commonly agreed diagnosis is the Rotterdam consensus where PCOS is diagnosed if two or more of the following are found:

- PCO morphology as observed on an ultrasound scan
- Androgen or male hormone related symptoms (see below) OR elevated male hormones in the blood
- Irregular or absent periods

The diagnosis also assumes that other conditions, which mimic this picture and sometimes are associated with polycystic looking ovaries, have been excluded.

## What are the symptoms of PCOS?

The following is a list of some of the possible symptoms and abnormal biochemistry associated with PCOS:

- Hirsutism (excessive hair growth on the face, chest, abdomen, etc.)
- Scalp hair loss (androgenic alopecia, in a classic "male baldness" pattern)
- Acne
- Polycystic ovaries (seen on ultrasound)
- Infertility or reduced fertility
- Irregular or absent menstrual periods
- Elevated LH level
- Elevated testosterone level (or other androgens)

In addition, some women with PCOS appear to be at increased risk of developing the following health problems during their lives:

- Insulin resistance
- Diabetes
- Cholesterol (lipid) abnormalities
- Cardiovascular disease (heart disease, heart attacks and stroke)
- Endometrial carcinoma (cancer)

Infertility may be a consequence of PCOS but is often not necessarily an issue, particularly if there is a strong focus on maintaining a lean body shape and an active lifestyle. Women with PCOS should use contraception when not desiring pregnancy. PCOS women with abdominal weight gain will often recommence regular



ovulatory menses with more exercise and weight loss. It is important to recognise appropriate waist measurements and BMI for different ethnicities. For example, Asian and Indian women often have metabolic changes and irregular cycles due to PCOS at a lower BMI than a person of European descent.

There are two physical appearances (phenotypes) of PCOS women – lean and overweight. Lean women with PCOS will often have symptoms from puberty. Heavier women with PCOS may be relatively asymptomatic in their teens while maintaining a fit and lean physique and only develop menstrual irregularity when a more sedentary lifestyle after school leads to weight gain and less overall exercise and activity. Immigrant women often present with this history. PCOS can be associated with longer-term risks, including diabetes, raised blood pressure, abnormal cholesterol, sub fertility and cancer of the uterus. Mostly these can be avoided or delayed by a healthy lifestyle, such as non-smoking status, maintaining a strong exercise ethic, avoiding weight gain, and checking health with your general practitioner on a regular basis. Periods should arrive every 3 to 5 weeks and longer cycles should be reported. Women with a family history of diabetes need to be extra cautious.

#### Warning signs – when to seek help

- Cycles shorter than 3 weeks or longer than 5 weeks
- No periods at all
- Unwanted hair growth
- Jawline acne

#### **Causal Factors**

We don't really know what causes PCOS and it seems unlikely to be just one factor. Genes do matter – brothers and sisters of women with PCOS often have similar changes in their blood tests. Weight gain exacerbates abnormal androgen levels and symptoms.

#### **Medical Treatment**

The condition of PCOS is managed rather than cured. Early diagnosis is encouraged. Women with PCOS are advised to maintain significant levels of exercise and a slim body mass index (BMI) (ideal BMI is 20-22) so that the risks of diabetes and subfertility are minimised. A diagnosis of PCOS should be sought in women with persistent acne and allows judicious use of anti-androgen therapy. Anti-androgen therapy (except for metformin) cannot be used if conception is desired but can provide significant relief from excessive hair growth and recurrent acne otherwise. Anti-androgens are best used in combination with physical methods of hair removal and always need effective contraception in conjunction.

Very lean PCOS women may need assistance to ovulate and there are several interventions, which are useful (clomiphene, metformin, and ovarian diathermy). Usually a fertility specialist would assist the general practitioner in this situation, and more complex assisted technology is not often required. PCOS women should be aware, however, that they may be more at risk of pregnancy related-complications, especially gestational diabetes.

For PCOS women who need ovarian stimulation treatment with gonadotrophins, such as for IVF treatment, ovarian stimulation can be more complex to manage than with non-PCOS women. Sometimes the difference in drug dose between giving rise to under stimulation and overstimulation is very fine, and can vary from one cycle to the next. Women with PCOS also have a higher risk of Ovarian Hyperstimulation Syndrome (OHSS), which is the most common (and potentially serious) side effect of IVF treatment. IVF drugs and procedures are often adjusted to allow for this increased risk in PCOS women.



Contributed by Dr Stella Milsom, Fertility Associates

## Self Help Dietary and Lifestyle Guidelines

- Lose weight there is a link between obesity and PCOS, and studies show that losing weight (in all but very lean women) may be the best way to treat PCOS. An important Australian study showed that a 10% weight loss often leads to improvement of menstrual cycles and return of ovulation. A study in Fertility&Sterility (2009) compared the effect of clomiphene, metformin and lifestyle modification on treatment of patients with PCOS. It showed that the highest clinical pregnancy rate was achieved with lifestyle modification. Waist circumference, insulin and lipids were also lower in the lifestyle modification group compared with the other groups on the drug regimes. The authors conclude that lifestyle modification proves to be the first and foremost way of dealing with PCOS.
- Follow a low glycaemic index diet this not only helps in weight-loss, but may help to prevent problems with blood sugar levels and insulin-resistance, which are also implicated in PCOS. A glycemic index diet is an eating plan based on how foods affect your blood sugar level. Carbohydrate-containing foods have a number assigned to them, according to how much each food increases blood sugar. The purpose of the low glycemic index diet is to eat carbohydrates that are less likely to cause large increases in blood sugar levels, which ultimately can cause insulin resistance, which in turn can cause the hormonal disturbances seen in PCOS. More can be read in the following study http://www.ncbi.nlm.nih.gov/pubmed/23999280
- **Exercise regularly** this will aid in weight loss and maintaining healthy weight, as well as helping to regulate blood sugar levels.
- Foods to increase to achieve weight loss
  - High fibre-containing foods: oats, brown rice, nuts, seeds, flax, psyllium, unpeeled fruits and vegetables; these will help you feel full on less food and help regulate blood sugar levels.
  - Fresh fruit and vegetables, especially berries, leafy greens, and brightly coloured vegetables: do not consume more than 1 or 2 serves of fruit per day as they can disrupt blood sugar levels.
  - Foods high in essential fatty acids Omega 3 in particular (oily fish, flaxseeds, pumpkin seeds, walnuts).
  - Healthy protein sources such as chicken, fish, lean meat and vegetable protein sources such as nuts, seeds, legumes. Protein is important in the regulation of healthy blood sugar levels

     include a source of protein at every meal.
  - o Eat small meals frequently to stabilise blood sugar levels
- Foods to minimise
  - Foods containing refined carbohydrates (white flour, white rice, white pasta, white crackers etc) - these foods have a high glycemic index and can contribute to elevated blood sugar levels, insulin resistance and obesity
  - Sweet foods and sugars
  - High fat foods, especially saturated fats: these can contribute to obesity
  - Alcohol has a very high glycemic index and can cause elevated blood glucose levels

Contributed by Loula George, Fertility NZ and Mother-Well Holistic Health



## RECURRENT MISCARRIAGE

## What is Recurrent Miscarriage?

Miscarriage is defined as a pregnancy that ends spontaneously before 20 weeks gestation. In NZ it is estimated that one in five known pregnancies end in miscarriage. These rates may be even higher as many miscarriages go unrecognised because they occur before a woman even knows she is pregnant. The majority of miscarriages occur in the first trimester. Once eight or nine weeks are reached and the baby's heartbeat is seen on a scan there is only 4-5% chance of a miscarriage. The risk then continues to drop as the pregnancy proceeds.

Most pregnancy losses are sporadic, non-consecutive spontaneous miscarriages that occur as an isolated event. Recurrent miscarriage, also known as Recurrent Pregnancy Loss (RPL) classically refers to the occurrence of three or more consecutive losses of clinically recognised pregnancies prior to the 20th week of gestation. By this definition, approximately 1% of couples will experience recurrent early pregnancy losses. This is greater than expected by chance alone suggesting that in at least some of these couples, a specific cause can be found.

## **Symptoms**

Most miscarriages are diagnosed once a woman reports to her doctor with vaginal bleeding and cramping lower abdominal pain. These symptoms are caused by the separation of the degenerating placental tissue from the uterine wall and the contractions of the uterus to expel the products of conception through the cervix. The alternative presentation is the finding of a nonviable pregnancy on ultrasound, which had been performed to check the gestation, or when there are reasons for concern, for example the loss of pregnancy symptoms or the uterus being smaller than expected for the calculated time of gestation.

## **Causal Factors**

With the frequent occurrence of miscarriage, theories on potential causes abound and a large number of studies have been performed searching for a cause, but it would be naive to believe there to be one or only a few. Aetiology of RPL includes:

- **Genetic factors** for example, structural or numerical chromosomal abnormalities such as chromosomal translocations. Found in 3-5% of couples with RPL compared with 0.7% of general population.
- **Anatomical factors** congenital uterine anomalies such as a septate uterus, diethylstilbestrol-linked anomalies or acquired uterine anomalies such as intrauterine adhesions, fibroids, polyps, incompetent cervix are associated with RPL.
- **Endocrinological factors** uncontrolled diabetes mellitus or thyroid disease, possible association with polycystic ovarian syndrome or Hyperprolactinaemia
- *Immunological disorders* an abnormal maternal immunological adaptation to pregnancy has been proposed as a cause of miscarriage for over 50 years. This is a controversial area especially regarding the natural killer cells test which has yet to be fully understood or to consistently and reliably



diagnose such a problem. The Antiphospholipid syndrome is the only proven autoimmune disease associated with RPL.

- **Thrombophilias** There is a large and contradictory literature on the association between inherited thrombophilias (genetic tendency to form blood clots) and RPL. However, there is evidence to suggest such conditions such as factor V Leiden and other blood clotting conditions could play a part.
- Lifestyle factors Miscarriage is more common in women who are significantly under or overweight, women who smoke or drink large amounts of alcohol or caffeine. Advancing maternal and paternal age is also associated with increased rates of miscarriage. Various environmental factors have been implicated over the years, e.g. VDU screens, anaesthetic agents in theatre nurses, general pollution, air travel, saunas and Jacuzzis, sex, stress none with proven scientific bases.
- **Unexplained** In at least 50% of couples, no explanation or reason will be found for their recurrent pregnancy losses

## **Evaluation of RPL**

This is an evolving and controversial area. If you have had three miscarriages in a row, tests will be offered to try and ascertain the cause. Testing is not usually offered after one or two early miscarriages, but you may be offered tests after two early miscarriages if you are in your late 30s or early 40s, or if it has taken you a long time to conceive. In general the following tests should be considered:

- Karyotypes of both parents +/- products of conception from miscarriage
- Assessment for uterine abnormalities with pelvic USS, HSG, sonohysterogram, MRI, laparoscopy or hysteroscopy
- Testing for the Antiphospholipid syndrome (anticardiolipin antibodies, lupus anticoagulant, B2GP1 antibodies – positive if levels significant on two or more occasions at least 12 weeks apart)
- Thyroid antibodies/TFT's
- Ovarian reserve testing (basal FSH, antimullerian hormone, antral follicle count)
- +/- additional tests as indicated by history e.g. thrombophilia screen, prolactin, DNA sperm fragmentation

#### Unproven tests for RPL, but used by some practitioners:

- TORCH screen, routine vaginal/cervical swabs
- Tests for diagnosis of immune-based RPL e.g. HLA typing, peripheral blood NK cell levels, cytokine polymorphisms
- Endometrial biopsy
- ANA
- Screening for diabetes
- Progesterone assays
- Homocysteine levels
- MTHFR polymorphisms

#### **Management of RPL**

 Couples with RPL require empathy and understanding. Early pregnancy loss is an emotionally traumatic experience, similar to that associated with stillbirth or neonatal death. In addition, RPL is one of the most frustrating and difficult areas in reproductive medicine because the aetiology is often unknown and there are few evidence-based diagnostic and treatment strategies. Emotional support is important in caring for these couples, and may enhance therapeutic success.



- In just over half the couples no specific cause is found, so called "unexplained" RPL. In these couples, attention to lifestyle factors and early pregnancy support and monitoring through the first trimester of the next pregnancy is offered. The chance of a subsequent successful pregnancy in these couples is ~70-75%.
- Couples where an underlying cause for their RPL is found are offered specific treatment to help improve their chances of a live birth in the future. For example, if a genetic abnormality is found, pregnancy chances may be improved with assisted reproductive techniques such as IVF with preimplantation genetic diagnosis or use of donor gametes. In patients with proven Antiphospholipid syndrome, live birth can be improved with the use of anticoagulation in a subsequent pregnancy. Some women with an anatomical abnormality may be offered surgical correction or if this is not possible, may consider a gestational carrier (surrogate). Despite lack of evidence for causation, many "immunological treatments" have been trialed but none have been shown to be effective and some may be harmful.

Contributed by Dr Karen Buckingham, Repromed; Auckland Recurrent Pregnancy Loss Clinic

## Self help

Living a healthy lifestyle before you get pregnant improves your chances of having a successful pregnancy and a healthy baby. Preconception health care can be undertaken for the 3-4 months prior to conception. This can include the following:

- Aim to reduce the intake of processed and refined foods as these are often of poor nutritional value. A diet based on vegetables, legumes, fruit, whole grains, lean meat, poultry, fish and dairy foods is recommended
- Ensure that the supplementation of important nutrients essential to a healthy pregnancy are in place prior to conception i.e. folic acid, iodine, prenatal multi, omega 3 oils , vitamin D (if deficient)
- Stop smoking and taking any recreational drugs
- Reduce alcohol and caffeine
- It is important to ensure you get adequate rest and relaxation. Let go of all daily non-essential activities and concentrate on your own well-being first. A degree of stress in your life is inevitable, but how you deal with it is important
- It is best to be at a healthy weight when you become pregnant. Being overweight or underweight puts you at increased risk for problems during pregnancy. Healthy food choices and physical fitness, together, can help you reach or maintain a healthy weight
- Get your health and medications evaluated have any medical conditions such as diabetes, epilepsy, obesity and high blood pressure treated and kept under control before becoming pregnant and throughout pregnancy
- If you have had two or more miscarriages, have a discussion with your GP about doing some medical investigations/tests

Contributed by Loula George, Mother-Well Holistic Health

## **Emotional impact**

It is normal to experience a number of feelings following a miscarriage as women respond to the loss of their pregnancy, their hopes and dreams for their future. Miscarriage is a very real loss but as it does not appear as tangible as other losses, (i.e. There is no formal ceremony to mark the loss) this can mean it is sometimes not acknowledged by others or minimized and consequently women can question their grief. The experience of miscarriage is unique; women have different physical, emotional and spiritual experiences and responses to miscarriage so no one way is the 'right way '. A Woman that has experienced her 5<sup>th</sup> miscarriage following a series of fertility treatments may feel quite differently than another woman's experience of miscarriage. It



is important not to compare your response to others because everyone's situation and story is different. Whatever your response to your loss is reflects your unique experience so that is completely okay.

Common responses to miscarriage are: an overwhelming feeling of sadness, disappointment, devastation, emptiness, guilt about the loss; perhaps there was something you thought you could have done to prevent it, perhaps you feel responsible that you were unable to carry your baby to full term, shame that you do not seem to be able to do what you may see other women can do easily, anger that your pregnancy ended when you were so careful and had tried so hard when others conceive unexpectedly, trauma about the physical experience of the miscarriage or medical treatment you have had for your pregnancy loss, worry and anxiety about the thought of it happening again, feeling cheated that you could not celebrate your pregnancy, fear about the future and if you will ever have a child, frustration and confusion that there are no answers. These are only just a few responses, there are many, many more.

Those that experience the loss of miscarriage time and time again can struggle with a number of things in their journey; the accumulation of loss, the feeling that this may never end, the longing for a pregnancy but the fear that they may miscarry again, difficulty with making a decision about when to stop trying, frustration and sadness that you feel unable to celebrate your pregnancy, anxiety when you are pregnant, the experience of depression, re-experiencing the loss of previous miscarriages, anger, frustration and confusion and even suspicion that the cause of your miscarriages are unknown, the loss of intimacy in your relationship, the feeling that you and your partner are worlds apart in your feelings and experience, the feeling that you may be burdening your partner or others around you as the loss continues on. Again this is only a few of the many responses for those experiencing recurrent miscarriage.

#### What can be helpful in a RPL journey

- Give yourself permission to grieve
- Allow yourself to feel the feelings
- Find ways of acknowledging the loss with a ceremony, symbol or letter to your babies or a drawing if you think this would be helpful
- There is no time period for grief. It is a journey that changes with time so be realistic rather than setting expectations around when you 'should feel better'.
- If you think you need help with your loss and the impact on your relationship or life, speak with a counsellor who understands this journey
- Tell someone who wants to listen to your story
- Take care of yourself; eating, sleeping and exercise routines will help you to feel in control
- Men and women grieve in different ways and are impacted by miscarriage differently.
- It is normal for women to feel the impact of miscarriage intensely and for a prolonged period because the loss is physical and emotional
- Talk with your partner about the differences in your experiences you don't have to feel the same way, you just need understand and accept that you have different feelings
- Keep the communication with your partner open and seek support from a counsellor if you need help to understand each other.
- Be open about what you need with others let people know if you want to talk about it or if you don't.
- Take control of the things you can making a plan with the doctor about treatment and investigative testing, looking after yourself.
- Try to have another goal or other projects even if they are small ones, maybe a hobby.
- Make a plan about the length of time you wish to try for a pregnancy but also be prepared to review it



• Give yourself time to grieve the loss of your pregnancies; it is natural to feel empty and want to try to get pregnant again but it is important you feel you have the emotional resilience if the pregnancy does not continue and that you feel ready in your grief journey.

It helps to remember that the intensity of your grief will change and you will feel better with time. Grief is a natural and normal response to loss and allowing yourself to grieve will help in your healing and coping with your emotions.

Contributed by Megan Downer, Fertility Plus

LINKS http://www.miscarriagesupport.org.nz/ http://www.fertilitynz.org.nz/information/fertility-fitness/





## What is Unexplained Infertility?

'Unexplained infertility' is a common phrase in the reproductive world. It is the term used when there is no cause found for infertility. A diagnosis of unexplained infertility is given to about 15-25% of couples with infertility. It does not necessarily mean that there is no cause – rather, it may mean that the cause has just not been found.

Infertility may be said to be unexplained if the woman is ovulating regularly, has patent fallopian tubes with no adhesions or endometriosis, if the man has normal sperm parameters and the couple have been having frequent intercourse at the time of ovulation for at least one year. The final diagnosis is made only after all the necessary tests have been performed and all results are found to be normal.

## **Diagnosis of Unexplained Infertility**

Although normally investigations are commenced after 12 months of unprotected intercourse without conception, in couples where the woman is more than 35 yrs old most doctors will recommend commencing investigations after 6 months.

Investigations should include a semen analysis, assessment of ovulation and ovarian reserve, a pelvic ultrasound (female) and tubal patency check by hysterosalpingogram or laparoscopy.

The most accurate way currently to assess ovarian reserve is a serum Anti Mullerian Hormone (AMH) assay. This blood test can be performed at any time of the menstrual cycle and should be very helpful in determining ovarian reserve and likely ovarian response if treatment with ovarian stimulation is recommended.

## Treatment

A couple with unexplained infertility still have a fairly good chance of getting pregnant on their own, without needing treatment at all, although this will be dependent on the age of the woman and the length of timing trying to conceive to date.

The principal treatments for unexplained infertility include expectant management with timed intercourse and lifestyle change, clomiphene citrate or letrozole with or without intra uterine insemination (IUI), lipiodol tubal flushing, and IVF.

#### **Expectant Management and Lifestyle changes**

Cigarette smoking, abnormal BMI, and excessive caffeine and alcohol consumption can reduce fertility in the male and female partner. Both partners should be counselled to achieve a normal BMI and reduce caffeine intake to less than 250mg (2 cups) daily. The age of the female partner will impact the chance of expectant management being successful

Lipiodol or Laparoscopy

Lipiodol tubal flushing and /or the laparoscopic treatment of mild endometriosis with tubal flushing have been shown in some studies to help couples with unexplained infertility conceive.

Your fertility specialist can discuss these options with you and recommend them if appropriate



#### Clomiphene citrate

The use of Clomiphene with timed intercourse in patients with unexplained infertility has been shown to only have a small benefit – probably 40 cycles of empiric clomiphene are required to achieve one extra pregnancy

> IUI

Intrauterine insemination involves placing washed prepared sperm in the uterine cavity at ovulation either on a natural cycle or with stimulation. A recent Cochrane review confirmed that IUI with stimulation increased the live birth rate when compared to IUI alone

> IVF/ICSI

This is the most effective treatment for unexplained infertility where simpler options have been unsuccessful. IVF will also give an explanation for the infertility in some couples. Many IVF clinics recommend ICSI (sperm microinjection) as part of the IVF cycle for long term unexplained infertility, or a 50/50 IVF/ICSI split for inseminating follicles

#### Summary

A thorough and timely investigation of couples is required before making a diagnosis of unexplained infertility. Various treatment modalities are available with maternal age and length of infertility with current ovarian reserve (as determined by AMH) being the best predictors of success.

Contributed by Dr Guy Gudex, Repromed

#### Self Help

In cases of unexplained infertility it is important for both partners to try and achieve optimal health. Dealing with any health issues (either managing or resolving) can give couples an opportunity to understand if those particular health problems were having an impact on their fertility. A preconception health programme can benefit couples with this diagnosis by ensuring that other factors that they have some control over, i.e. nutritional, lifestyle, environmental factors and stress, are dealt to in a way that enhances their overall reproductive health. This will have the added benefit of helping to ensure a healthier pregnancy as well. It is very important to see your GP and/or specialist for guidance regarding investigative tests in order to attempt to understand possible causal factors.

Contributed by Loula George, Fertility NZ and Mother-Well Holistic Health