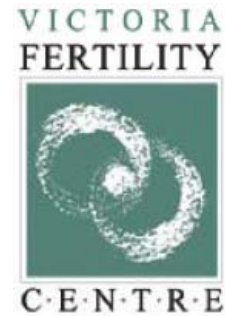


## **SUBFERTILITY ASSESSMENT AND MANAGEMENT**



### **INTRODUCTION:**

Approximately 15% of couples will experience difficulty conceiving – and seek help. Although the number of couples who are unable to have a child is considerable, infertility remains a very personal issue. The suffering and despair which childlessness may bring to an otherwise healthy relationship may be very substantial.

A healthy fertile couple in their early twenties, having regular intercourse, have an approximately 20-25% chance of conceiving every month. This means that around 9 out of 10 couples trying to have a baby – with no other health issues – will conceive within one year. Statistically, as we get older, the chance of conceiving and having a successful pregnancy declines. As mentioned above, the best that Nature can do, is a healthy young couple in their early twenties for a successful pregnancy rate of 25% per cycle.

With the progress made in assisted reproductive technology (ART), we prefer not to use the term infertility – but rather subfertility. Many couples who we were previously unable to help – we are now able to assist with such techniques as superovulation, intrauterine insemination (IUI), in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI).

There may be many reasons why a couple are not able to achieve pregnancy. In some cases there may be one obvious single cause, however, in many there are two or three “subtle” reasons – which may independently not seem important, however, when added together contribute towards the problem. Therefore, in many cases there are factors in both the male and the female – reminding us that it is important to remember that this is a couple problem.

### **REVIEW OF THE FEMALE REPRODUCTIVE SYSTEM**

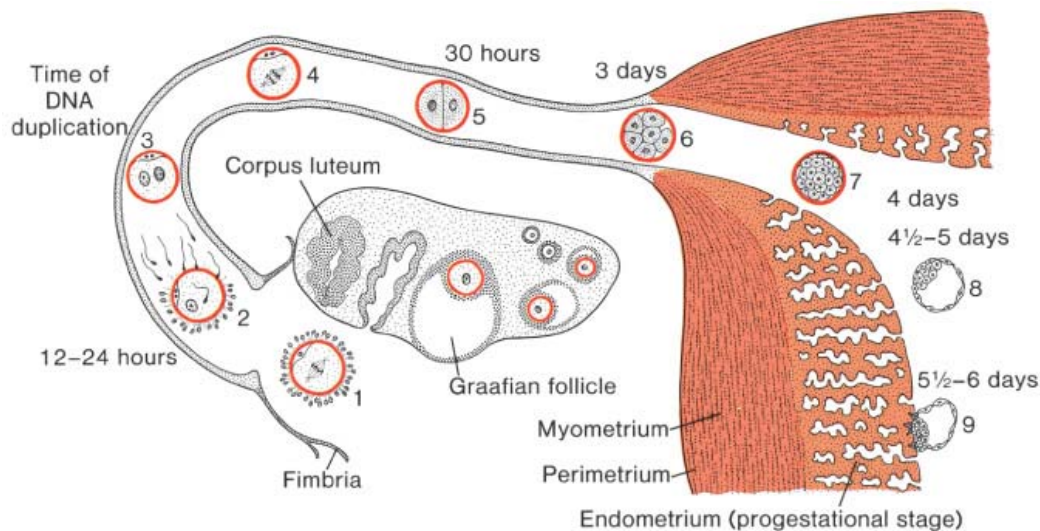
A female is born with all the eggs that she will ever produce. These are stored in an immature form in her ovaries. The total number of eggs that are available to a woman in her early teenage years is between 150,000 and 300,000. At the beginning of each menstrual cycle the ovaries receive a hormone signal in the form of FSH (follicle stimulating hormone) from the pituitary gland in the brain. In response to this message, hundreds of eggs in the ovaries respond to the call. However, 99% of these do not develop and die after a few days. A few eggs continue to mature in a small capsule of fluid called a follicle. In most cases only one of these will develop to full maturation – with the follicle reaching a size of about 18-20 mm. As this egg matures in its follicle, it produces a hormone called estrogen, which is monitored by the brain. This estrogen level peaks as the egg reaches maturity, and at this time the brain releases another hormone signal (luteinizing hormone – LH) which triggers the ovary to release the egg. If all goes well, after the egg is released from the ovary it is captured by the end of the fallopian tube (fimbria) and travels into the tube itself.

## Subfertility – Assessment and Management

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After the egg is released from the ovary, a little cyst called a corpus luteum is formed to make a hormone called progesterone. Unless a pregnancy occurs – this little corpus luteum cyst has a life span of only 14 days. During these 14 days the progesterone produced nurtures the lining of the uterus (endometrium) and helps support an early pregnancy. If the egg is fertilized by a sperm in the fallopian tube, an embryo is formed. The embryo spends a few days traveling down the tube, then arrives in the uterus and implants in the carefully prepared endometrium. If a pregnancy does not occur, after 14 days the corpus luteum dies, and there is no more progesterone support for the lining of the uterus, and menstruation occurs.

The whole cycle then occurs over again.



### **FACTORS TO BE CONSIDERED:**

#### **□ Age**

With advancing age there is increased risk of infertility, spontaneous miscarriage and genetic abnormalities (such as Down's syndrome). As mentioned earlier, the best that Nature can do is a successful pregnancy rate of about 25% per cycle for a healthy young couple in their early twenties.

For women aged between 30 and 35 years, with no other medical problems, the best pregnancy rate per cycle would be 15 - 20%, however, with a miscarriage rate of about 15%.

For women aged between 36 and 39 years, the best pregnancy rate per cycle would be 10-15%, with a miscarriage rate around 23%.

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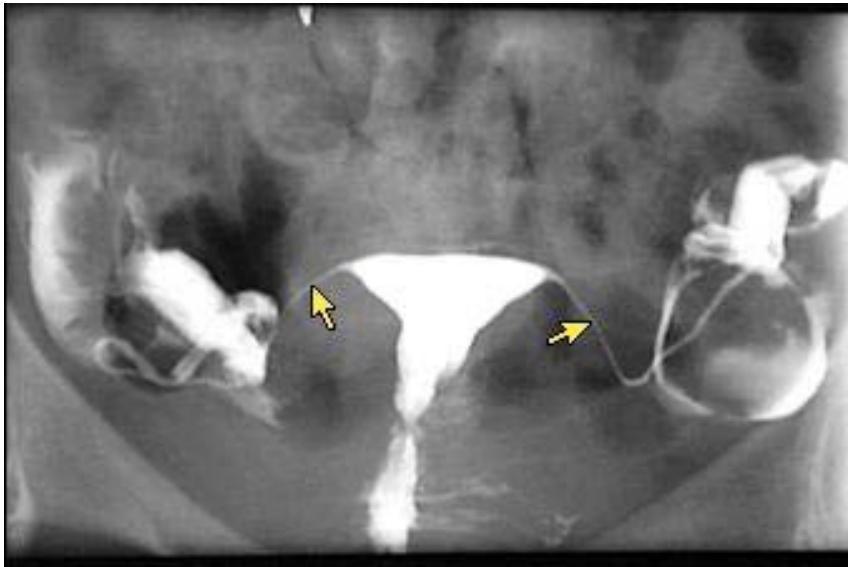
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### □ Uterus and fallopian tubes

In order for the eggs and sperm to meet and successfully fertilize, the fallopian tubes must be patent and functional. The uterine cavity must also be healthy to allow implantation of the embryo. Different ways to assess the uterus and tubes include hysterosalpingogram – or direct methods which involve looking inside the uterus (hysteroscopy) and inside the pelvis (laparoscopy). Hysterosalpingogram involves an x-ray procedure, with injection of dye through the cervix and x-rays to check for filling of the uterus and spill of dye from the fallopian tubes. Hysteroscopy and laparoscopy are surgical procedures which may involve a general anesthetic in an operating room. A telescope is then inserted through the cervix into the uterus. A laparoscopy involves inserting a small telescope through the umbilicus to allow examination of the internal organs.

Hysterosalpingogram



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### □ **Male Factor**

The quantity and quality of sperm is very important. This would be assessed by doing a test called a semen analysis. The male will be asked to abstain from masturbation or intercourse for at least 72 hours, and then ejaculate into a small sterile container – to be delivered to a specific laboratory which handles semen. There are a number of factors which are evaluated – and these include the volume, liquefaction, the sperm count, as well as the motility and morphology (shape) of the sperm.

### □ **Hormone Factors**

Sometimes there may be a mild imbalance in hormones which can influence fertilization and implantation. These factors may either cause infertility or early recurrent miscarriages.

### □ **Immune Factors**

We all have a defense mechanism called the immune system. This is designed to protect us from foreign proteins. However, sometimes our immune system malfunctions in a very subtle way – your immune system may be evaluated by doing certain blood tests.

### □ **Pelvic Factors**

Occasionally there are problems in the female pelvis which can influence fertility. Tubal blockage and scarring from previous subclinical infection is a fairly common problem.

Photograph of a Hydrosalpinx. ( a swollen and damaged tube)



Another common condition is endometriosis. This occurs in approximately 20 to 25% of women who are experiencing difficulty getting pregnant. In this condition, endometrial cells which normally line the inside of the uterus (endometrium) grow in distant sites. Endometriosis refers to the growth of this tissue outside of the uterus. The most common sites for this tissue to grow are on the ovaries, fallopian tubes, bladder, pelvic side walls and rectum. Symptoms associated

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with endometriosis are very variable. There may be no symptoms at all. On the other hand, some more common symptoms include pain with intercourse, painful periods, and spotting before periods (premenstrual spotting). Endometriosis is diagnosed by doing a laparoscopy. Treatment may be either medical or surgical.

### **□ Cervical Factors**

The cervix is the entrance to the uterus. It produces a clear and friendly mucus at the time of ovulation. This mucus nurtures the sperm and allows entry into the uterus. The function of the cervix can sometimes be affected by previous surgery (such as a cone biopsy) or by inflammatory changes.

### **APPROACH AND INVESTIGATIONS:**

1. Careful history.
2. Clinical examination.
3. Pelvic ultrasound.
4. Blood tests.
5. Semen analysis.
6. Hysterosalpingogram.
7. Laparoscopy/hysteroscopy.
8. Specific tests as indicated.

### **MANAGEMENT:**

Management will obviously depend on what factors are identified during the evaluation. Some options for management include the following:

#### **1. The use of fertility drugs.**

These are also known as ovulation induction agents. There are a variety of drugs which are used to stimulate ovulation (egg production) These drugs may be either taken by mouth, or given by injection. These drugs are used to induce ovulation in women who are not ovulating regularly, but they are also used in women who are ovulating – in the hope of encouraging the release of more than one egg to assist in getting pregnant. (i.e. egg harvesting)

There may be a variety of side effects associated with the use of these drugs. There may also be a risk of multiple pregnancy.

#### **2. Surgery.**

In certain circumstances surgery is necessary for the treatment of conditions such as pelvic scarring, endometriosis, endometrial polyps and uterine fibroids.

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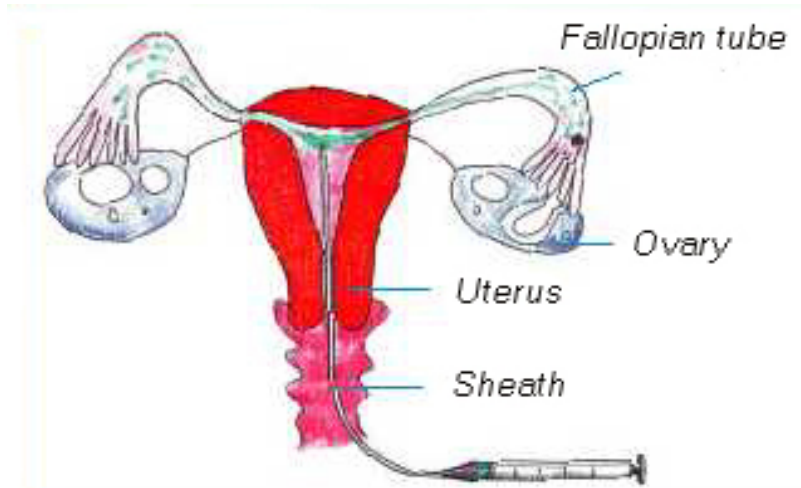
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### **3. Intrauterine insemination.**

When the sperm parameters are not optimal – fertility may be enhanced by using a combination of fertility drugs and timed intrauterine insemination of washed sperm.



### **4. In vitro fertilization.**

In vitro fertilization is a very successful way to treat subfertility. This is a complicated and sophisticated form of management, which involves stimulating the ovaries with fertility drugs. During this process the ovaries are monitored by regular ultrasound examinations. As mentioned previously, the eggs mature in little capsules of fluid called follicles which are easily tracked by ultrasound. Blood tests may also be used to check the level of estrogen. When the eggs are ready a drug is given to mature them, and they are then retrieved by ultrasound guidance. During this process a needle is passed through the vagina into the ovaries, and the eggs are sucked out. The eggs are then fertilized with sperm outside of the body. If the sperm quality is not good, the sperm can be injected into the egg to force fertilization. This process is called intracytoplasmic sperm injection (ICSI). After three or four days, the embryos are then evaluated, and the best quality embryos are put back into the uterus. This involves passing a very small catheter through the cervix into the uterus – and depositing the embryos. This is called embryo transfer.

The overwhelming factor affecting the success rates of in vitro fertilization is a woman's age. For women under the age of 35, the success rate is approximately 50 – 60% per completed IVF cycle where at least 2 embryos are transferred.. For women aged between 35 and 40, the success rate is between 30 and 40% if two good quality embryos are transferred, and for women aged between 40 and 45, the success rate is lower, at between 20 and 35%.

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### **RISKS OF OVULATION INDUCTION:**

#### **1. Multiple pregnancy.**

There may be a risk of multiple pregnancy associated with the use of fertility treatments. Early ultrasound will identify how many pregnancies are in the uterus. If there are more than two, the risks of premature labour related to triplet or quadruplet pregnancies is significant. In this case a procedure called selective reduction is available. This is usually done at between 10 and 12 weeks' gestation, and involves sacrificing one or more embryos, thereby reducing the number of surviving embryos to two. It is done by passing a small needle into the uterus in a fashion similar to an amniocentesis. There is a risk of miscarriage associated with this procedure – in the region of around 5%.

#### **2. Hyperstimulation syndrome.**

Fertility drugs may sometimes unexpectedly cause an excessive number of eggs to mature in the ovaries. If this occurs, high doses of estrogen are produced – and these can be measured in the bloodstream. These high levels of estrogen may under certain circumstances cause a condition called ovarian hyperstimulation syndrome. This can be associated with the leakage of fluid into the abdominal space (peritoneal cavity) and chest. The condition can be rarely life-threatening (as can pregnancy!). It is usually self-limiting though sometimes requires specific management. This management may include tapping excess fluid from the peritoneal cavity or chest, and the use of intravenous proteins called albumin. It usually only develops if there is a pregnancy – because of the extra high levels which occur as soon as an embryo implants in the uterus.

#### **3. Ovarian cancer.**

There has been some suggestion that there may be a link between the use of fertility drugs and ovarian cancer. There have been a number of studies evaluating this risk – and at the present time, although it is not absolutely clear, there does not appear to be a definite risk between the use of fertility drugs and ovarian cancer. Risk factors for ovarian cancer include – family history, diet, and childlessness. Protective factors include pregnancies and birth control pill use. In other words, it is a very confusing problem to sort out. Women who never achieve a pregnancy, or who choose not to become pregnant, have a higher risk of ovarian cancer than women who have pregnancies. Although recent studies from Israel are very reassuring that there is probably not an association between the use of fertility drugs and ovarian cancer – it is still prudent to use drugs in a cautious and responsible fashion.

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