



GENERAL INFERTILITY BOOKLET

Barbados Fertility Centre

MISSION STATEMENT

Our professional medical team will provide you with a world class service while seeking to minimise the stress associated with IVF and maximising the potential for a successful outcome.

Background to Mission Statement

Our philosophy at Barbados Fertility Centre is BALANCE. We believe a balanced approach to everything in life is always the most successful approach. At Barbados Fertility Centre we have carefully balanced high quality medical care from an excellent medical team with our promise to provide our very best to deliver a positive outcome. Providing this balance ensures patients get the best possible care while minimising their stress levels. Infertility is a stressful time for couples and many studies reflect the negative impact this has on success. We are committed to reducing these stress levels for our couples and making this journey an easier one, while behind the scenes our specialist medical and laboratory team are providing the most up to date and expert technologies available. In summary, at Barbados Fertility Centre we provide a world class medical service combined with personalised care.

CONTENTS

Introduction

The Clinic

Section I Reasons for Fertility

- Ia Basic Steps
- Ib Female Infertility
- Ic Male Infertility
- Id Unexplained Infertility

Section II Evaluation of Infertility

- IIa Basic tests

Section III Treatment Options

- IIIa Ovulation Induction
- IIIb Intrauterine Insemination
- IIIc In-Vitro Fertilisation
- IIId Intracytoplasmic Sperm Injection
- IIIe Additional Aspects of ART Treatment

Section IV Embryo Freezing

Section V Donor Gametes

- Va Donor Sperm
- Vb Donor Egg Program

General Pregnancy Advice

Frequently Asked Questions (FAQ'S)

Conclusion

Introduction

Infertility is generally defined as a couple's failure to achieve a pregnancy after one year of regular unprotected intercourse. This definition is based on expected monthly conception rates of 20-25% among healthy young couples and studies demonstrating that 85% of normal couples conceive within one year. However, one in six couples or 15 % of couples will not achieve a pregnancy within twelve months of trying for a baby.

The causes of infertility can be extremely simple or very complex. Over the last few decades there have been many advances in our understanding of the causes of infertility and of treatment options. In addition, the development of tests that are better able to evaluate potential causes for a more effective treatment plan. Together with scientific advances and new technologies, fertility treatments today are now more effective than ever.

Over the last two decades the number of couples who have infertility has increased. Probably the greatest cause of this increase is that women are delaying starting their family for a number of reasons: second relationships, career and educational demands, desire for financial stability, waiting for a stable relationship etc. Also, general awareness of infertility and the different treatment options means that couples are also more likely to come forward to seek assistance with their quest for a baby.

Often one of the hardest aspects for a couple who are trying for a baby is to accept that perhaps they might have a problem. The next step is to seek advice from experts. Remember for all other aspects of medical problems specialists exist who can help. Infertility or subfertility is no different. Unfortunately many couples choose to ignore the problem. In the majority of cases the problem doesn't go away, instead can become more complex.

Remember the most significant predictor for the success of achieving a pregnancy is the maternal age. For women, their fertility decreases steadily from 35 onwards. Sadly for some women this age related decline may start from some years before. Options exist, so take steps to avail of these and towards your dream of getting pregnant and having a family.

THE CLINIC

Barbados Fertility Centre specialises in all aspects of infertility management. We were founded in 2002 to meet a growing demand from Caribbean patients for a full time IVF unit and a growing demand from international clients for IVF services that combine the advantages of high quality medical care with a more relaxed atmosphere in the Caribbean.

Our team approach

Barbados Fertility Centre provides a team approach to your care. Throughout your treatment with us, a highly specialised team of doctors, nurses and embryologists will manage your care individually, to provide the best possible outcome. They are highly skilled individuals who provide support, education, information and management. This is a step by step journey which we are happy to walk with you. While we deal with solving fertility every day we also realise that this is a unique event in your life and should be respected as such in all our dealing with you.

Appointments

All appointments can be made by calling+ (246) 435-7467 or email caustrie@barbadosivf.org

For first / initial consultations please remember to specify to the receptionist that your appointment is for fertility - as special arrangements are made for such an appointment. This appointment will take approximately 45 minutes.

Subsequent appointments are made accordingly.

Blood tests/ semen analysis/ other tests: Most tests are performed at Barbados Fertility Centre, unless otherwise arranged. Every effort is made to make these as convenient as possible for our patients.

If you are unsure or have any questions please contact one of our nurse co-ordinators and they will happily assist.

Hours

Our opening hours are Monday to Friday 7.30am to 4pm.

Emergencies: Fortunately emergencies are rare in infertility. However, if you need to contact us after hours (for emergencies only) call BayView Hospital (246-436-5446) and ask for Dr Skinner to be paged.

I REASONS FOR FERTILITY PROBLEMS

The causes of infertility can be varied and in many cases a combination of factors may be identified. Statistics show that in couples where a cause can be identified, female factors account for approximately 40% of all infertility cases, male factors account for a further 40% and in the remaining 20% of cases there is a combination of female and male factors. Sometimes a minor problem with both partners when combined is enough to impair fertility, even though the couple may have had no problems in other relationships. For some couples despite investigation, the underlying reason for infertility remains unexplained.

Ia BASIC STEPS OF HUMAN REPRODUCTION

The human reproductive process is complex. A number of steps need to take place in order for a pregnancy to occur. These can be simplified as below:

- The ovary must develop a follicle (fluid filled sac within the ovary) within which there is an egg / ovum.
- A mature ovum (egg) must be released from the ovaries (ovulation).
- The egg must be caught by the fallopian tube and drawn into the end of the tube (ampulla region).
- Adequate numbers of spermatazoa must be deposited 'at or near' the cervix around the time of ovulation. The sperm must swim up through the female tract to meet the egg- first through the cervix, then the uterus and finally down one of the fallopian tubes to meet the egg.
- Once at the egg the spermatazoa must penetrate the outer capsule of the egg (zona pellucida) and thus fertilise the egg.

- After fertilisation the egg is called an embryo. Whilst early development of the embryo is taking place the delicate cilia which line the tube are beating to move the embryo towards the womb or uterus.
- The uterus needs to be receptive to the embryo and allow implantation. Implantation usually occurs 3-5 days after the egg is fertilised.

Ib FEMALE INFERTILITY

There are many different causes of female infertility. Sometimes more than one minor cause is present and collectively then is enough to create a problem.

The female reproductive tract consists of 2 ovaries, 2 fallopian tubes, a uterus (womb), cervix (neck of the womb) and vagina.

Causes of infertility in a woman may be divided according to the anatomical level at which the problem lies. The sort of problems that may occur at each level is set out below:

OVARIAN

Anovulation

Anovulation means the failure of the release of the egg from the ovary. Overall this is the most common cause of female fertility problems (40%). In 'normal' menstrual cycles hormones are released from the pituitary gland (in the brain), which induce follicular formation which allows the egg to finish its development and eventually to mature. Once mature, the egg is released or ovulation occurs. In 'normal' circumstances one egg is released per month.

If an egg is not released, pregnancy cannot occur. There are a number of reasons why ovulation may not occur. The most common reason is the presence of polycystic ovaries (PCO), which are described below. Other hormone imbalances may be associated with a failure of ovulation such as hyperprolactinaemia or thyroid dysfunction. Extreme weight changes may be enough to stop ovulation. As women get older the ovaries may become more and more resistant to the hormone stimulation, which induces normal ovulation.

Polycystic Ovarian Syndrome (PCOS)

Polycystic ovarian syndrome is a condition in which there is a hormonal imbalance within the ovaries. It is a complex condition. In PCOS, the ovaries are bigger than average, and the outer surface of the ovary has an abnormally large number of smaller follicles. In PCO these follicles remain immature, which means that ovulation rarely happens and so the woman is less fertile.

Women who have PCOS may have the following problems: 1) infertility due to lack of ovulation, 2) excessive body hair growth (hirsutism) due to imbalance between hormones, 3) irregular menstrual cycles and heavy bleeding (cycles which are either less than 21 days or more than 35 days apart) due to lack of ovulation, 4) acne and 5) obesity. Some women with PCOS may have a higher than normal miscarriage rate if they become pregnant.

However, all of these symptoms are not present in all patients with polycystic ovaries. The condition represents a spectrum of problems. Regular cycles may occur in 40% of women with PCO. Many women with PCO have no additional hair growth and some women are underweight!

While it is not known if women are born with this condition, PCO seems to run in families. Ongoing research is trying to clarify whether there is a clearly identifiable gene for PCOS. Women

are also at a risk when overweight. Maintaining weight or body mass index (BMI) below a critical threshold is probably very important as weight loss improves hormonal abnormalities and improves the likelihood of ovulation and thus pregnancy.

The diagnosis of PCOS is made primarily on the woman's presenting history and examination. The diagnosis can be confirmed on ultrasound or by measuring the woman's hormonal levels.

Because PCOS can lead to a resistance to insulin it has been shown that women with PCOS will respond better to fertility treatments if they are treated concurrently with *Metformin* (a type of drug known as an "insulin-sensitising agent" which lowers the blood sugar level, in turn reducing the excessively high insulin). Studies suggest that it may well be useful in several areas: helping weight reduction, normalizing blood cholesterol and improving irregular periods (70%) leading to ovulation. The most common side effects during treatment on *Metformin* are diarrhoea, nausea, vomiting and abdominal bloating.

In very resistant cases of PCOS an operation called ovarian drilling, performed by laparoscopy, can also be used to treat women with PCOS. During this procedure the ovary is cauterized by drilling into it in a number of spots.

TUBAL

Tubal factors account for 20% of explained causes of infertility. The fallopian tube is the road along which the sperm and egg usually meet. Either blockage of the pathway or impairment of the function of the tube can cause a woman to be infertile.

The function of the fallopian tubes is delicate. It is partially dependant on the close proximity of the tubes to the ovaries. But also dependent on the ability of the tube to move closer to the area on the ovary from which the egg will be released. The inside of the fallopian tubes contain tiny hairs or cilia, which by beating are able to suck the egg into the end of the tube and so "catch" the egg. The inside lumen of the tube must be open to allow the sperm to make their way down the tube to the egg. After fertilisation the cilia are responsible for moving the embryo (which cannot move on its own) back up the tube to the uterus / womb.

Previous infection or inflammation of the fallopian tubes may damage both the ability of the tube to move due to the formation of scar tissue and also the ability of the cilia to beat or function. In addition, this damage may actually block the tube and thus prevent the sperm and the egg meeting at all! Infection is the most common cause of tubal factors. Infection may occur as a result of pelvic inflammatory disease (PID) but may also be secondary to other nearby infections such as appendicitis. Any procedure involving the inside of the womb such as a D&C, an endometrial biopsy, a termination of pregnancy etc, carries a risk of pelvic infection.

Tubal blockages may occur secondary to endometriosis (see below) or because of previous surgery. Ectopic pregnancy (a pregnancy that implants in the tube) will result in damage of the tube.

Very rarely congenital defects of fallopian tube formation occur. This may result in the absence of one or both fallopian tubes.

UTERINE

Abnormalities of uterine anatomy or function may cause infertility. These may include leiomyomas (Fibroids), endometrial polyps, foreign bodies (e.g. an IUD), intrauterine synechiae (scar tissue), congenital malformations and chronic endometritis (infection).

It is felt that these conditions may cause a failure of implantation due to mechanical interference and/or a functional impairment of normal endometrial growth and maturation.

Fibroids

Fibroids are benign (non-cancerous) growths of the muscle of the uterus (womb). They are sometimes called myomas, fibromyomas or leiomyomas, but most people call them fibroids. Fibroids are common – around 20% of women get them. Fibroids can affect the shape and internal environment of the uterus. They can make it more difficult to conceive but they only account for about 3% of the total cases of infertility.

Fibroids are most common in women in their 40s and 50s, towards the end of the reproductive years. They are more common in women of Afro-Caribbean origin, who also tend to be affected at a younger age.

There are different types of fibroids, named according to where they are found:-

- Intramural fibroids are found within the muscular wall of the uterus.
- Subserosal fibroids grow outwards from the outside wall of the uterus. They can become very large.
- Submucosal fibroids grow from the inner wall of the uterus and can take up space inside the uterus. These account for only 5% of all fibroids.

Fibroids grow very slowly. They can cause symptoms as they grow bigger, but even so, at least half of all fibroids cause no problems at all. The most common symptom / sign of a fibroid is heavy periods.

Up to half of all women with fibroids have heavy periods. In some cases this can lead to anaemia. As fibroids get bigger they may cause pressure related symptoms such as lower abdominal discomfort or backache, or may press on the bladder causing symptoms such as needing to pass urine more often than normal. The uterus may also press on the rectum causing constipation. Some women experience pain or discomfort during sexual intercourse (dyspareunia) because of fibroids. The problems that fibroids may cause depend on their location.

It is estimated that fertility problems are one of the presenting features in about ¼ of women with fibroids. There is a well-established relationship between the presence of fibroids and lower fertility. When compared to other causes of infertility, however, they are a relatively uncommon cause, being implicated in only 3% of couples. It may be that a delay in having children (whether voluntary or involuntary) predisposes to the development of fibroids and this is more often an association rather than a causative feature.

The diagnosis of fibroids is most accurately made by ultrasound (U/S). Whilst pelvic examination may flag the diagnosis U/S allows the fibroids to be characterised according to the size, number and type. By using techniques which allow the uterine cavity to be evaluated, such as SIS, HSG or hysteroscopy, it is possible to determine whether the fibroid(s) affect the cavity or internal lining of the uterus/womb. This is particularly important with respect to fertility. If the fibroid affects the cavity then it may be necessary to remove the fibroid prior to fertility treatment. On the other hand if the fibroid does not block a tube or affect the cavity there is no benefit to removing it.

Endometrial polyps

These are like skin tags of the womb. These are easily detectable by Saline Instillation Sonogram (SIS).

Congenital abnormalities

A variety of abnormal uterine shapes exist. The more minor variations of uterine shape such as a heart shaped uterus or bicornuate uterus may exist in as many as 3-5% of women. These more

common anomalies are very rarely associated with infertility. More serious, and less common, types include full bicornuate uterus, unicornuate or even the double uterus. These may affect the implantation of a pregnancy and may cause miscarriage or preterm labour.

CERVICAL FACTORS

Abnormalities of either cervical mucus or the cervical canal itself may affect fertility. During the fertile time of the month the mucus changes and facilitates the passage of sperm. In some cases a negative cervical mucus-sperm interaction may occur and be a cause of infertility.

Cervical stenosis (blockage or narrowing) may present an obstacle to the passage of sperm into the uterus and therefore, onwards to the egg. This may be a result of previous surgery - such as a cone biopsy or cryotherapy, which are commonly used in the treatment of abnormal Pap smears.

OTHER FACTORS

ENDOMETRIOSIS

Endometriosis is a condition where clumps of endometrial cells (the tissue of the lining of the womb) exist outside of the womb. Despite the condition being recognized for over a century it is still not fully understood. Most women with endometriosis do not have any problems. However, some women may experience pain and others infertility. But yet some fertile women have endometriosis!

Potentially, endometriosis may exert a negative effect on fertility by causing any of the following:

- Adhesions or scar tissue between the tube and ovary, which stops the tube being able to move around freely (to catch an egg) and perhaps impairment of tubal function internally.
- Growth on or in the ovary may upset the hormone milieu within the follicle and so affect the health of the egg.
- Large collections of endometriosis in follicles may lead to endometriomas or 'chocolate cysts'. These cause pain, may necessitate surgery and even by just being there may stop the ovary from functioning correctly.

Endometriosis is best diagnosed by laparoscopy (where a camera is inserted into the umbilicus which allows the internal pelvis to be visualised). Ultrasound may also allow diagnosis if endometriomas exist on the ovary.

There are many treatments for endometriosis. The aim of medical agents is to stop menstruation and so lead to the drying up of the clumps of cells / endometriosis. Medical treatments include GnRh analogues, depot progesterone, OCP (given continuously), Danazol etc. Surgical techniques include laser or diathermy to endometriosis deposits and removal of endometriomas.

Infertility related to endometriosis, is often treated by In Vitro Fertilisation (IVF). However, this treatment is usually not first line and is dependant on many other factors.

AGE AND FERTILITY

The number of couples in their late 30s and 40s attempting pregnancy is increasing. Currently 25% of patients at Barbados Fertility Centre are aged 40 or over. However it is important to

remember that fertility in women declines with age, particularly in the late 30s and 40s. This is a normal part of the ageing process.

As women become older, the chance of becoming pregnant is lower, the chance of having a miscarriage is higher and there is an increased risk of chromosomal abnormalities in the baby. In the general population, the chance of becoming pregnant after the age of 40 is estimated to be only 5% per cycle compared to about 25% per cycle in the under 40 age groups.

One-third of couples where the woman is over 35 will have fertility problems. Treatments such as IVF cannot reverse the effects of age on fertility, but do help as more eggs are obtained per cycle and therefore the chance of developing a healthy embryo is greater per cycle with IVF, compared to a spontaneous conception cycle.

The reason for the age related decline in fertility is multifactorial. Females are born with all their eggs and never make a new egg. This compares to men who make sperm from cells on a continuous basis. Girls are born with about 400,000 eggs in their ovaries. The eggs are matured and ovulated during each menstrual cycle. For every egg that is released many more degenerate and are re-absorbed into the body. Eventually the ovary does not respond to the hormones that mature and release eggs and the woman experiences menopause. Because the eggs are present in the ovaries from birth, they age along with the woman, reducing their quality.

Other factors such as the prevalence of fibroids, cysts, endometriosis, previous pelvic infection etc all have a potential negative effect on fertility. As women get older these conditions become more common.

Ic MALE INFERTILITY

Male infertility is very common. About one in twenty men are sub fertile and a male factor is present in 40% of all infertile couples. About one third of all assisted reproduction (ART) procedures are performed for male factor infertility. For most men the discovery that they are infertile comes as a total surprise.

The testis has two distinct roles. The first is to produce the male sex hormone, testosterone, which is important for providing sex drive, erections, strong muscles and basically giving a man a general feeling of well being. All these things can be described as virility. The second function of the testis is to produce millions of sperm everyday, a process that occurs inside each testis. For most infertile men it is only this second process that is at fault so hormone levels and thus virility is normal but the sperm count is abnormal.

Most infertile men produce low numbers of sperm, which may also show both poor swimming ability (called motility) and be abnormally shaped (morphology). In such men, only a small number of normally shaped motile sperm are likely to swim up the woman's fallopian tube into the vicinity of the egg and even then may be unable to fertilise the egg.

Why does this problem develop? We now believe that most cases (66%) are genetic. In other words, these men are born without the genetic information that would allow sperm production to occur normally. Therefore until a genetic treatment is developed (if ever) sperm production cannot be improved. Assisted reproduction techniques (ART), in particular ICSI, offers the best chance of success as much fewer normal sperm are required than in nature.

In the remaining one third of infertile men, a likely cause for their infertility may be identified:

1. Obstruction to the passage of sperm from the back of the testis to the outside can result from blockage or absence of the vas deferens. Common causes include, obviously, vasectomy, but any history of injury, and other surgery or sexually transmitted disease may be important.

2. Men can make antibodies to their sperm following vasectomy or other trauma or infection. These antibodies are a common cause of infertility and prevent sperm swimming or sticking to the egg. Such antibodies can only be found using a special test on a fresh semen sample.
3. The testis can be damaged by a wide number of treatments including chemotherapy or repeated X-Ray therapy.
4. Some men have difficulties obtaining an erection, or in ejaculating due to a wide range of problems such as diabetes, MS, or previous prostate surgery. In these cases sperm can be found and used for IVF.
5. Rarely, a deficiency in the brain pituitary hormones may result in low sperm counts. Its detection is important as it is readily treated with hormone injections.

Despite many advances less than 10% of male infertility can be overcome by medical or surgical techniques. In the remainder treatment is best by ICSI. Even men with extremely low sperm counts can father a child when ICSI is used.

Id UNEXPLAINED INFERTILITY

Despite thorough investigations in approx. 20% of couples no clear cause of infertility may be found. A careful systematic approach is taken to investigations. Should a diagnosis not be reached after these it does not mean “nothing is wrong” but that the potential problem cannot be investigated by simple means.

Two specific areas fall into this category. Tubal assessment by conventional methods only allows a basic anatomical assessment. It does not guarantee the full functional ability of tubes. So even with a normal tubal assessment it is possible that tubal problems may be present that may prevent conception.

Full gamete (sperm or egg) assessment is only possible through in-vitro fertilization where the gametes are observed and evaluated. So if the cause of infertility remains unexplained the best step is to proceed to an IVF cycle, which has the advantage of being both diagnostic as well as therapeutic at the same time.

II EVALUATION OF INFERTILITY

Over the years there have been many advances in diagnostic tests for infertility. Each test is specifically chosen to help identify different potential causes. By carefully timing tests we gain as much information about fertility as possible with each test.

Initial Consultation

The first consultation is with one of our Consultant Gynaecologists, where a full history is obtained for both the male and female. This includes past medical and surgical history, previous pregnancy history (if any), current menstrual history and a detailed account of any evaluation or treatments previously performed.

A detailed description of fertility and potential causes is reviewed. Any specific relevant aspects of the couple's history is brought into this discussion.

At the end of this consultation a treatment plan will be made that is relevant to the individual couple. For many patients the next step will be evaluation or investigation of potential causes. In

the event that a diagnosis has already been made or confirmed, then these couples may proceed straight to ART.

N.B. A referral is not mandatory. It is useful to have copies of any relevant previous test reports. However, if needed, we can arrange these after your first consultation. We do try not to repeat tests unnecessarily but as a general rule if the test has been performed over a year before, it is likely that a repeat test is warranted, depending on the test type and result.

IIa BASIC TESTS

A number of carefully chosen tests are performed to collectively assess different aspects of the steps of reproduction. These need to be carefully timed to the menstrual cycle to gain the best interpretation. As a general rule all of these can be carried out within one menstrual cycle from the first consultation. After the initial investigations are completed we will be able to best provide you with an effective and individualised treatment plan.

FEMALE

Hormone blood tests

- a) **Baseline female Gonadotrophins:** FSH, LH, Estradiol
These are done on day 2 or 3 of the menstrual cycle. These evaluate ovarian function.
- b) **Mid-Luteal Progesterone.** This is taken approximately 7 days prior to the onset of menstruation (ie usually day 21 if the woman has a 28 day cycle). It is used to evaluate if ovulation has occurred.
- c) **Prolactin.** This hormone rises normally in pregnancy and breast feeding but if it is elevated outside of pregnancy it can prevent ovulation and pregnancy occurring.
- d) **Thyroid Function.** TSH is used to assess thyroid dysfunction as this may cause infertility. Although an uncommon cause of infertility, if present medical treatment of the thyroid dysfunction will usually correct fertility.

Monitoring Ultrasound: A Transvaginal ultrasound, done between day 10 -12 of a cycle, allows an accurate assessment of ovarian function. This test is also used to assess response to treatment.

Saline Instillation Sonography (SIS): The uterus and ovaries are evaluated by U/S (as above). A speculum is then passed and the cervical canal assessed. A small catheter is passed through the cervix all the way to top of the womb. The cavity length is measured. Fluid is then put through the catheter, which allows the cavity of the uterus and the tubes to be evaluated. This test allows an accurate assessment of both uterine and tubal factors.

MALE

Semen analysis: The basic semen analysis provides information on semen volume and sperm concentration, motility (movement) and morphology (shape). The World Health Organisation standard results for normal semen analysis are set out in Table 1.

Table 1: World Health Organisation criteria for a normal semen analysis

Characteristic	Value
Volume	1.5-5.0ml
pH	>7.2
Sperm Concentration	>20 million / mL
Motility	>50%
Morphology	>14% Normal

III TREATMENT OPTIONS

IIIa OVULATION INDUCTION (OI) AND CYCLE MONITORING

As the name suggests, ovulation can be induced with the aid of medical treatment. The most common agent used is *Clomiphene Citrate or Clomid®*. It is a tablet administered for 5 days at the beginning of the menstrual cycle (usually day 2-6). It is a highly effective treatment - 80% of patients with anovulatory infertility will become pregnant within 6 cycles/months of treatment.

It is very important that the effectiveness of the treatment is assessed. This is done by performing a transvaginal ultrasound on day 12 of the menstrual cycle. Some women will require higher doses of *clomid®* before the ovaries will respond.

If despite increasing doses of oral ovulation induction medications, the ovaries still do not respond then treatment with low dose *Gonadotrophin* injections can be tried (*Menopur®*, *Puregon®*). Cycle monitoring with ultrasound is also performed on all cycles with *Gonadotrophins*.

Risks of ovulation induction cycles include:

1. Side effects of agent used: Occasional (10%) - hot flushes, nausea, headache, bloating, breast tenderness and rarely hair loss or visual disturbances.
2. Multiple Pregnancy: With oral agents the risk of multiple pregnancy is 5-10%. Nearly all multiple gestations will be twins. (Rates are higher with usage).

If the anovulation is caused by PCO, sometimes a better response may be obtained by using other types of oral ovulatory agents such as *Tamoxifen*.

IIIb INTRAUTERINE INSEMINATION (IUI-H)

Intra Uterine insemination involves the insertion of the male partner's semen into the female partner's uterus in order to improve the chances of pregnancy.

The female partner's menstrual cycles are tracked with ultrasound scanning to optimize the correct day for insemination. Ovulation induction with clomiphene or gonadotrophin injections is usually used, especially if the woman does not have regular menstrual cycles. Once ovulation is confirmed, the male partner is asked to produce a semen sample by masturbation. The specimen is prepared so that the normal active sperm are separated into a culture media. This prepared sample is then placed high up into the woman's uterus by means of a fine catheter.

This procedure potentially treats cervical factor female infertility. It may also be beneficial for mild male factor infertility. However, is very unlikely to be successful in more severe male factor problems.

The success rate for this procedure is 10 – 15%.

IIIc IN VITRO FERTILISATION (IVF)

IVF literally means fertilisation outside of the body. The technique was pioneered through the 1970's by Patrick Steptoe and Professor Robert Edwards. Since the birth of Louise Brown, the first test-tube baby in 1978, IVF has resulted in over 1.5 million babies worldwide. Pregnancy rates and live birth rates have improved over the past few years, leading to a steady increase in the number of IVF treatment cycles performed worldwide.

There are several groups to whom IVF treatment may be advised that include:

- Women with blocked or damaged Fallopian tubes, inoperable tubes or whose tubes have been removed after ectopic pregnancies.
- Women with endometriosis.
- Women with ovarian disorders.
- Men with infertility problems.
- Couples with unexplained infertility.

Steps of IVF

IVF essentially involves four main steps.

1. Ovarian stimulation: The woman is given fertility medications to stimulate her ovaries to produce many follicles; the small fluid filled structures, which develop in the ovary. Each follicle should contain one egg. The chances of pregnancy are increased if more than one egg can be obtained and fertilised.

During this phase the development of the follicles is monitored using blood tests and by visualizing the ovary by ultrasound.

2. Egg retrieval: The eggs are collected from the follicles using the vaginal ultrasound probe with an attached guided aspiration needle under sedation/local anaesthetic.

3. Insemination: On the morning of the egg-collection, the man produces a sperm sample by masturbation. The best sperm are then selected using a sperm wash technique and each egg is inseminated with prepared sperm. The eggs are inspected for signs of fertilisation the next morning.

4. Embryo Transfer: Embryos are placed into the uterus using a small catheter. This is usually performed 3 days after egg retrieval.

N.B. If an excess of embryos are present on the day of embryo transfer these can be frozen to be used at a later stage. About 30% of couples have embryos remaining to freeze. (See section on FET)

POSSIBLE RISKS OF IVF TREATMENT

These can be divided into medication, procedure and general risks.

Medication risks:

The medications used for ART are known to create some minor side effects in women. There is no evidence of increased risk to a baby born as a result of a properly managed treatment. Side effects include: headache, nausea, mood changes and injection site reactions.

Ovarian Hyperstimulation Syndrome (OHSS)

All women undergoing ovarian stimulation, such as during an IVF treatment cycle, experience enlargement of their ovaries and a complex change in their hormone balance. The condition is often marked by bloating, as excess fluid is retained.

For up to 5% of stimulated women this can be quite unpleasant with abdominal bloating and pelvic discomfort, however, for <1% of stimulated women, the abdominal pain and fluid retention is so severe that admission to hospital can be necessary. Symptoms may include marked abdominal swelling, nausea, vomiting and diarrhoea, lower abdominal pain, and shortness of breath. Hyperstimulation varies in severity and rarely requires treatment in hospital, but you must contact the Barbados Fertility Centre if you notice any of the above symptoms so that we can monitor you closely.

"Ovarian Hyperstimulation Syndrome" (OHSS), usually presents a few days after embryo transfer.

Severe symptoms require:

- bed rest
- correcting the fluid imbalances with an intravenous drip
- relieving pain and nausea
- injections of heparin to counter the tendency of the blood to clot abnormally.

Fortunately this condition is self-limiting. It usually resolves after several days, with a natural excretion of the abnormal accumulation of fluid, however it may persist for weeks, especially if a pregnancy has been achieved. This condition will not effect the pregnancy outcome.

On **rare** occasions very serious complications have been associated with OHSS.

Failed Ovarian Stimulation

Occasionally (1 in 1500) the ovary will fail to respond to stimulation with Gonadotrophins for IVF. A number of factors influence your medication dose and regime for ovarian stimulation. If the ovarian stimulation is suboptimal then it may be best NOT to proceed to egg retrieval and repeat an IVF cycle using a higher dose or different regime.

Procedure Risks

Vaginal egg collection is a simple procedure usually done using conscious sedation so no anaesthetic is required. The patient is not in discomfort during the procedure. There is a small risk of bleeding (1 in 500) and infection.

Embryo transfer carries, minimal, if any risk.

General Risks

Success / Failure

IVF does not guarantee a pregnancy. Success rates vary with age, reason for infertility and other specific factors. We will give you an individual percentage chance of success. This will be reviewed with you, once all your tests are completed.

Multiple Pregnancy

ART or IVF carry a greater chance of multiple pregnancy. Overall worldwide statistics show that nearly 25% of IVF pregnancies will be twins, 2-3% triplets and 0.5% quads.

Multiple pregnancy carries significant risk to both mother and babies. In particular, high order multiple pregnancy (Triplets or more) is associated with a poor survival rates for babies (neonatal mortality is increased by 5-15 fold) and impaired long term function (e.g. cerebral palsy is increased 6 fold). It also places greater physical strain on the mother, with an increased incidence of miscarriage, high blood pressure, bleeding during pregnancy, increased risk of vomiting during pregnancy, and premature birth.

Consequently we at Barbados Fertility Clinic strive to balance the success of our treatments with possible multiple pregnancy. Thus as a general rule only 1-3 embryos will be transferred back to the uterus.

Miscarriage

ART does not increase the risk of miscarriage. Miscarriage rates do vary with age and are more common over 40.

Ectopic pregnancy

The incidence of ectopic pregnancy approximates that in the general population.

Birth Defects

It is important to remember that any medical or surgical treatment has risks, adverse effects and side effects. Couples should be aware that one baby in 20 born worldwide will have a birth defect. There is no clear evidence that infertility medicines, if properly used, increase this risk.

IIId Intracytoplasmic Sperm Injection (ICSI)

In a significant number of male factor couples, conventional techniques like IVF may not be possible due to a low number of motile sperm in the ejaculate. In other couples, IVF may no longer be a useful option because previous poor fertilisation rates imply a problem with sperm function. For this group, sperm microinjection (ICSI) provides the best means of achieving pregnancy.

The ICSI technique involves the injection of a sperm through both the zona pellucida and the wall of the egg directly into the centre of the egg. The procedure requires a great deal of technical skill in the picking up of individual sperm and their individual injection into the egg without damaging

the ovum. All procedures are performed under a microscope using a sophisticated micromanipulation system.

Following injection, the eggs are cultured and assessed for fertilisation in a similar way to conventional IVF. Like IVF embryos are transferred into the uterus three days later or frozen for later use.

Risks

All aspects discussed under IVF apply.

It is important to remember that ICSI is a relatively new treatment, the first children having been born in 1992. However, worldwide agencies collect data on the outcome of infertility treatments. Results to date do **not** indicate increased rates of abnormal pregnancy, miscarriage or birth defects (congenital malformations) in ICSI children. The only exception may be an increase in sex chromosome disorders such as Klinefelter's Syndrome.

As it is becoming more apparent that many cases of male infertility are genetic it is possible that these may be transmitted to future generations by ICSI. As boys inherit their Y chromosome from their father, they may have similar fertility problems later in life.

Long term assessment such as behavioral and intellectual outcomes of children born after ICSI is still ongoing. However, a number of studies have evaluated this and have not found any impairment

Success

Fertilisation and pregnancy rates are markedly improved with ICSI in severe male factor infertility (sperm counts less than 5 million/ml) and in patients with a previous history of failed IVF. In addition, men previously considered untreatable seem to have similar success, including those with completely immotile sperm, very abnormally- shaped sperm or those where sperm must be obtained from the testicle by surgery.

There is no doubt that ICSI has allowed men to father children who would previously not have been able to do so.

IIIe ADDITIONAL ASPECTS OF ART TREATMENT

Assisted Hatching

Before an embryo can implant it must hatch out of its "shell". In some cases this hatching may not occur. Assisted hatching is a procedure where the outer layer of the embryo is thinned or opened to facilitate hatching and therefore implantation.

In general it is used when the women is over 35 or if the FSH hormone level is elevated irrespective of age.

Blastocyst Culture

Conventional IVF involves culture or incubation of embryos for three days after egg retrieval. Embryos are then transferred to the uterus or frozen.

It is now possible with new culture media that embryos can be cultured for longer – 5-6 days.

Blastocyst culture has the following potential advantages

- It may better coincide with timing of implantation in nature.
- It potentially allows better selection of the strongest embryo for transfer.
- As fewer embryos are transferred at the Blastocyst stage it may reduce the incidence of multiple pregnancy.
- It may help identify a problem if patients have a number of failed IVF attempts.

Blastocyst culture does have potential disadvantages:

- The chance of having no embryos available for transfer is higher with Blastocyst culture than with standard culture (up to 25%)
- A higher than expected incidence of monozygotic twins (5%) have been reported.

IV EMBRYO FREEZING / CRYOPRESERVATION

It is possible to freeze embryos using special cryopreservation techniques. The first baby born in the world after transfer of a frozen embryo was in 1983. In 2003 Barbados Fertility Centre produced Barbados's first IVF baby resulting from embryos that had been frozen and thawed.

With current medical agents used to stimulate the ovaries for IVF or ICSI usually a number of eggs will be obtained. Although not all eggs will fertilise, and some embryos may stop developing before the day of transfer; for many couples a greater number of embryos than planned for transfer may be present. These embryos can be frozen for use at a later date.

Embryo Freezing

Embryos may be frozen between 1 and 7 days after egg collection. The majority of embryos at Barbados Fertility Centre are frozen on Day 3, by which time most embryos contain 4-8 cells.

The embryo freezing process takes approximately 3 hours. Embryos are sequentially treated with varying concentrations of a special solution, called the cryoprotectant. This solution protects the embryos during the freezing process. Each embryo is then drawn into a specially designed sterile straw that is labeled with the patient's full name, IVF number or date of birth, and the date of the freeze. The straws containing the embryos are placed into a freezing machine, slowly cooled to -35°C and stored in liquid nitrogen for long-term storage (-196°C).

Embryos may be held in storage for couples for up to 5 years.

Embryo Thawing

Embryo thawing is the reverse of the freezing process, and involves warming the embryos. Our Embryologist will thaw the embryos either the day before or on the day of the scheduled embryo transfer. Embryo thawing takes approximately 2 hours. Once the embryos are returned to room temperature, the embryos are again passed through a series of solutions to remove the cryoprotectant that is no longer needed. The thawed embryos are kept in the incubator until the embryo transfer, during which time they resume development and may undergo more cell division.

It is possible that some cells within the embryo may not survive freezing and thawing, however the embryo may still be viable. It is also possible that not all of your frozen embryos will survive the freezing and thawing process and in some cases no embryos survive freezing and thawing. There are currently no clear indicators to predict embryo survival. However the approximate survival thaw rate per embryo is 70%.

Patients are informed of the thaw results prior to admission. Your nurse coordinator will make every effort to contact you in the event that all your embryos have failed to survive the thaw.

Frozen Embryo Transfer (FET) cycle

FET can be planned with a spontaneous or normal menstrual cycle. In some patients concurrent hormone treatment is needed to prepare the lining of the womb for implantation of the embryo e.g. with *Clomiphene* or low dose *Menopur*.

An ultrasound scan is done to confirm adequate development of the uterine lining and to predict the optimal day for embryo replacement.

The day and time for FET is arranged and the embryo(s) are thawed accordingly. The actual embryo transfer is identical to that described in the section on IVF transfer (Section III).

The overall success rates associated with transferring frozen-thawed embryos are less when compared to a fresh embryo cycle.

V DONOR

In some cases it may become apparent that a severe gamete i.e. egg or sperm factor exists. Couples have just two choices if they wish to have a child – (1) adoption or (2) the use of a donor gamete.

Donor gametes mean that the couple are treated but the relevant gamete (ie sperm or egg) that is defective is replaced by a donor. Donor has the advantage that at least half the genetic make-up of the child comes from the relevant parent and the pregnancy can be shared by the couple. It should never be forgotten that the environment provided by the parenting couple has significant influence on the developing child.

Va DONOR SPERM

Approximately 1 in 25 males are unable to father a biological child for a variety of medical and genetic reasons. One in eight infertile couples require the use of donor sperm to achieve a pregnancy. Today, more couples are able to utilise microinjection of sperm (ICSI) with IVF but not all forms of male infertility are treatable with ICSI.

Should ICSI not be possible or if the couple chooses not to have ICSI for financial or personal reasons then Intra-uterine insemination with donor sperm (IUI-D) offers an alternative solution.

Pregnancies resulting from donor insemination have the same risk of complications during pregnancy and childbirth as the normal population and there is exactly the same risk of an abnormality in the child as with other pregnancies.

Selecting Donors for Couples

Non-identifying but relevant information about the natural characteristics of a donor is available for recipient couples to help choose a suitable donor. Each donor is given a code number and the non-identifying information available includes:

- nationality
- ethnic origin
- blood group

- physical characteristics - height, build, eye colour, hair colour, skin tone
- occupation
- level of education
- interests

Couples, under guidance from the clinic, select a donor whose characteristics best approximate the characteristics of the relevant partner. The aim is to have children who will not look out of place in their families.

The procedure is exactly the same as IUI as set out in the treatment options section.

Results

Treatment with thawed semen in women who have at least one open fallopian tube shows that 50-60% of women will be pregnant after 6-9 cycles – the equivalent of 6-9 months of treatments.

Vb DONOR EGG PROGRAM

The world's first baby conceived through egg donation was in 1984. Since then, hundreds of donor egg programs have been established throughout the world.

Although initially egg donation was used primarily to treat women who had a premature menopause (before age 40), more and more it is being used as an alternative as the female age increases and consequently success from conventional IVF reduces.

Egg donors may be:

- a. Altruistic - donating to the clinic for any couple and allocated by the clinic
- b. Known to the recipient couple
- c. Unknown to the recipient couple

Egg donors should be aged between 21 and 35 years, in overall good health and not be a carrier of any known genetic disease. Most donors today are fertile women who donate altruistically to a known or anonymous recipient. The known donor situation has the advantage that both identifying and non-identifying information is immediately available to both respective donor and recipient couples.

Treatment Cycle

Essentially Donor egg IVF involves the donor doing the first part of the steps of IVF (see IVF). Once the eggs are retrieved they are fertilised with the sperm of the recipient's partner. The embryos are then transferred into recipient.

Success Rates

The pregnancy rate of donor egg treatment by Barbados Fertility Centre approximates 35% cycle and is directly related to the number and quality of donated eggs. The follow-up of donor egg pregnancies worldwide has been extensively reviewed and shows no added risks or complications in the pregnancies compared to fertile women of similar age. The main problem for all donor egg programs today is the shortage of donors.

GENERAL ADVICE TO ENHANCE THE CHANCES OF BECOMING PREGNANT

At *Barbados Fertility Centre*, we have two goals for your treatment. The first is to help you become pregnant. The second is that you experience an uncomplicated pregnancy and deliver a healthy baby. Below is a list of things that you can do to help achieve these goals.

- **Stress**

Stress may be a significant contributor to infertility. For example, distress alone may cause anovulation – a condition where a woman does not ovulate at all. Struggles with infertility are a major source of stress. Research has shown that the stress of infertility is comparable to that for cancer, AIDS and other devastating illnesses. Barbados Fertility Centre recommends to all of our patients that by participating in our Mind/Body Program, they can cope better with the stress of infertility. Based upon medical studies it has been shown, that reducing stress may increase your success with treatment.

- **Smoking**

If you smoke, we recommend that you stop for general and reproductive health concerns. In addition to the detrimental effects on general health (e.g., heart disease, cancer, and chronic lung disease) smoking also has a negative impact on fertility. Women who smoke during pregnancy increase the risk of premature labor, decreased fetal growth and other complications.

- **Alcohol**

We recommend that if you are attempting pregnancy, you decrease your alcohol intake significantly. Alcohol can interfere with getting pregnant, and during pregnancy it increases the chance of birth defects.

- **Caffeine intake**

We recommend that you avoid caffeine altogether or limit intake to one caffeinated drink per day. Several studies have concluded that a woman's chance of becoming pregnant decreases while the likelihood of miscarriage increases when caffeine is ingested. Caffeine is present in coffee, tea, soft drinks and chocolate.

- **Recreational Drug Use**

The use of recreational drugs is inadvisable both while attempting to conceive and during pregnancy. Drug use by a woman during pregnancy, such as cocaine and heroin, may lead to severe withdrawal reactions in the baby after it is born. Some drugs, such as marijuana, has been shown to decrease sperm production. The use of intravenous drugs increases the risk of acquiring an HIV or hepatitis infection.

- **Medication Use**

You should discuss all medications that you are taking with your Barbados Fertility Centre physician. It is also important to contact the physician(s) who originally prescribed your medications to let them know that you are attempting to get pregnant. You should avoid taking non-steroidal anti-inflammatory drugs around the time of ovulation since these medications can interfere with ovulation and implantation. Paracetamol is a safe alternative. Taking herbal remedies should be discussed with your fertility specialist first, since their effect on fertility and pregnancy is unknown.

- **Body Weight**

Overweight – Abnormally high existing weight and/or increased weight during pregnancy creates a higher chance of complications during pregnancy, including diabetes, high blood pressure, and the formation of blood clots. Women who are overweight tend to have larger babies, more difficult deliveries, and are more likely to require a cesarean section. Cesarean sections performed on overweight women are associated with a higher incidence of anesthetic and surgical complications that could jeopardize the health of the mother and baby.

Underweight – It is believed that menstrual function requires a level of at least 22% body fat for normal menses to occur. Eating disorders and extreme exercise often result in an abnormally low Body Mass Index, and can contribute to metabolic and menstrual disorders, all of which are problematic for those trying to get pregnant. Research has shown that more than half of women who are underweight and then gain an average of 6-8 lbs, spontaneously conceive.

- **Vitamin Supplementation**

Folic Acid: We recommend that all women who are attempting to get pregnant take at least 0.4 mg (400mcg) of folic acid per day. Several studies have confirmed that folic acid supplementation started before pregnancy occurs will reduce the occurrence of neural tube defects in infants by almost 50%. (Neural tube defects are abnormal developments of the spine and skull, such as spina bifida). Multivitamins and prenatal vitamins containing folic acid are available over the counter and should be taken on a daily basis.

Vitamin A: Prenatal vitamins and over-the-counter-multivitamins contain a safe dose (5000 IU) of vitamin A. However, published data has confirmed that excessive intake of vitamin A increases the chance of congenital anomalies. We recommend that daily intake should not exceed 10,000 IU.

- **Exercise**

Moderate exercise during pregnancy has been shown to be beneficial. If you are already in an exercise program, we encourage you to continue. However, the medications used to stimulate the ovaries as part of your treatment can cause temporary large ovarian follicles. Therefore, we advise you to avoid high-impact activities (i.e. running, step aerobics). Also, extreme strenuous exercise may lead to a complete disruption of the menstrual cycle. Activities such as swimming, bicycle riding, walking, and using the treadmill are encouraged.

- **Nutrition**

Nutrition can also influence the achievement and maintenance of a pregnancy. In addition to a well-balanced diet, caloric intake should be limited to maintain a normal body weight. Foods with high content of fats and oils should be consumed at a minimum.

- **Routine Gynaecologic Care**

During your infertility treatment, it is important for you to continue your routine care with your gynaecologist or primary care physician. This care should include a yearly blood pressure check, physical examination, pelvic examination and Pap smear. After 40, a woman should have a mammogram every 1 to 2 years.

FAQ's

Do I need a referral letter to attend?

No referral letter is needed. Just call to make an appointment (246-435-7467) and specify that your appointment is for fertility. If you have had previous tests copies of the reports are helpful but again not mandatory – these can be arranged after the initial consultation, if necessary.

How do I arrange the tests?

Most tests are timed with the menstrual cycle. So once your period has started call the fertility nurse to schedule your test(s).

After the initial consultation how quickly can we proceed to treatment?

If further investigations are needed these can usually be arranged within one menstrual cycle. Once evaluation is complete then treatment cycles can commence with the next period.

If we need IVF how long does it take before we can start our treatment?

Once it has been decided that you need IVF there may be some routine testing required (see below). This must be completed at least 3 weeks prior to the first day of an IVF cycle. But once the bloods are taken we can schedule your cycle. Typically it is about 4-6 weeks between the start of medications and the replacement of embryos.

What routine testing is required prior to IVF at Barbados Fertility Centre?

All couples undergoing IVF at BFC require pre-cycle testing. A general list of these tests is available from the clinic but they do vary slightly depending on what treatment a couple is having. The list appropriate to you will be available after your initial consultation.

How many eggs should I expect to get with an IVF cycle?

Your in-cycle monitoring ultrasound scans will be able to give you an accurate count of how many follicles are developing. However, not every follicle always contains an egg. Usually about 80% of follicles yield an egg. The number of eggs collected is dependant upon each patient's response but at Barbados Fertility Centre our average egg number is 10 per retrieval.

Is IVF painful?

Some of the fertility medications are injections, which are administered subcutaneously with a short needle and discomfort should be tolerable. The egg retrieval is performed through the vagina with ultrasound and a fine needle. Patients at Barbados Fertility Centre are asleep during this procedure. The procedure is known as conscious sedation. This is not a general anesthetic but patients are not awake and they have no pain. They wake up very quickly after the egg retrieval, which usually lasts about 30 minutes.

The embryo transfer procedure is similar to a Pap smear or IUI procedure and is generally performed with minimal discomfort.

If my cycle is unsuccessful when can I have another one?

We recommend you take one month's break between **fresh** IVF cycles to allow the ovaries resume to normal before being re-stimulated. If you do have frozen embryos remaining from your fresh cycle however, you can choose to proceed with a frozen embryo transfer cycle without a break.

How long can my embryos remain frozen?

The HFEA in the UK, whose guidelines we follow at Barbados Fertility Centre, states that embryos can safely remain frozen for up to 5 years.

What activity restrictions should I follow after my embryo transfer?

Once you are discharged we recommend our patients rest the day of the embryo transfer procedure. Normal activities can be resumed the day afterwards. We do not recommend any high impact activities or over-exertion until the pregnancy test. We advise patients to avoid any hot-tubs/Jacuzzis or hot baths during this time also. Sexual intercourse can resume at any time depending on the female patients level of comfort after the egg retrieval.

I am on the birth control pill (BCP) and spotting – is this normal?

Yes, breakthrough bleeding is one of the most common side-effects of the pill. If you are having any bleeding or spotting and are concerned, phone your nurse coordinator. However, it is nothing to be worried about as the medication is still having the desired effect. You still need to continue the pill every day until directed by your clinic to discontinue.

Can my endometriosis affect my fertility or IVF cycle?

Endometriosis is a medical condition where cells that usually remain confined to the cavity of the uterus, grow outside of the uterus usually on or in the ovaries and also on the surface of the pelvic cavity between the uterus and the rectum. Endometriosis can cause pelvic pain and may also decrease the chances of natural conception, as it can affect tubal function and ovulation. Patients who require IVF and who have endometriosis should still have the same chances of a successful outcome as patients of the same age without endometriosis.

What about alternative treatments like acupuncture?

Acupuncture and Reflexology, administered by an experienced practitioner who is aware of your medical diagnoses and treatment plan, can facilitate relaxation as well as optimise ovarian response and implantation. We encourage our patients to seek assistance in these areas. Herbal medicines can be helpful but also potentially dangerous. We ask our couples to review any herbal medication with us prior to starting a course. They need to be dispensed under the guidance of an experienced practitioner.

FOR A FULL GLOSSARY OF TERMS PLEASE SEE OUR WEBSITE.

CONCLUSION

This booklet is intended to provide some information on infertility treatment. Hopefully it will help you make an informed decision about pursuing treatment with Barbados Fertility Centre.

BARBADOS FERTILITY CENTRE

www.barbadosivf.org

