PCRM Pacific Centre for Reproductive Medicine

Patient Orientation Guide

June 2016

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Pacific Centre for Reproductive Medicine – Edmonton Inc.
3rd Floor, 9888 Jasper Avenue, Edmonton, AB T5J 5C6
TF: 1 866 481 PCRM (7276) T: 780-990-4442 F: 780-990-4443 www.pacificfertility.ca

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Welcome to PCRM

Thank you for choosing Pacific Centre for Reproductive Medicine (PCRM) as your care provider. Our philosophy is simple yet important. We believe that our clients deserve to be treated with respect, dignity and privacy. We provide our patients with compassionate but highly effective reproductive care, by combining advanced reproductive technologies with a supportive and tranquil environment. Our multidisciplinary team consists of physicians, nurses, embryologists and administrative staff who work diligently to deliver the highest level of care to our patients. The team is dedicated to the assessment, planning, implementation and evaluation of your fertility treatment.

Patient education is an important part of your care and treatment. This guide will help you to understand your fertility issues and the methods we use to achieve conception. The guide was designed to address issues that are relevant to each stage of fertility care, as well as give patients an overall review of what is involved. As such, you may wish to read all of this material or only specific sections at this time. We recommend that you keep this guide as a valuable resource and refer to it when you are close to embarking on specific treatments.

Please remember that the information contained in this guide is quite general, and specific treatment protocols may vary depending on individual factors and treatment history.

Our Mission

To deliver excellence in fertility treatment and early pregnancy care.

Our Vision

To provide comprehensive care for all our patients while achieving the best possible outcomes.

Clinic Hours

The Pacific Centre for Reproductive Medicine is open from Monday to Friday between 7:30 am and 4:30 pm. Enquiries about your care are addressed between 9:00 am and 4:30 pm. If you feel you need to see a nurse or physician, please call the clinic in the morning so that we can accommodate your request for the same day. On weekends and holidays, the clinic is open between 8:00 am and noon. For emergencies, after hours, please contact the on-call physician at 780-990-4442.

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Treatment Monitoring Guidelines

All blood work and ultrasounds required to follow the progress of fertility treatments are performed at PCRM seven days a week. Patients are served on a first-come first-served basis, and patients are required to arrive no later than 7:30 a.m. Ultrasound examinations are performed following the blood test. You do not need a full bladder for these ultrasounds, unless otherwise instructed by a nurse or physician. You may eat or drink prior to either of these tests.

Upon arrival at the clinic, you will be required to present yourself to the reception desk for registration. Government issued photo identification is required for all monitoring and procedural visits, by partners when providing sperm samples, or when signing consents for services.

Treatment Reminders

We suggest that you:

- Stop smoking at least 2 months prior to treatment, and reduce or eliminate exposure to second-hand smoke.
- Ensure that you are getting between 0.4 mg and 1.0 mg of folic acid daily, in either a multivitamin or prenatal vitamin. Patients that are at a higher risk of having a child with a neural tube defect should take 5 mg of folic acid daily.
- Exercise regularly and eat a balanced diet.
- Have regular intercourse or ejaculation as advised throughout your treatment cycle (1-2 times per week), but not within 2 days of providing sperm sample for us.
- Keep the following medications refrigerated: Puregon®, Gonal-f®, Lupron®, and Ovidrel®.
- Ensure that your Pap smears are up to date.

We suggest you AVOID:

- Consuming more than 1-2 alcoholic beverages per day. After embryo transfer or intrauterine insemination, we recommend complete abstinence from alcohol until the results of your pregnancy test are known.
- Excessive exercise during the latter stages of your stimulation cycle and for about 1 week following egg retrieval. We suggest you also avoid high impact activities such as aerobics, jogging and horseback riding.
- Taking ASA (Aspirin) or ibuprofen (Advil, Motrin) products during your treatment cycle without discussing first with a PCRM physician or nurse.
- Starting or stopping of any medication that we have prescribed, unless you have been advised to do so by a PCRM physician or nurse.
- Initiating any other medical or complimentary (e.g. herbal) therapies without informing your PCRM physician or nurse.

Note: Many fertility treatments are uninsured medical services, and as such, the patient is responsible for the fees related to each. The clinic requires full payment for treatment prior to its initiation. In the event of cycle cancellation, fees are based on services received up to time of cancellation. We recommend that you retain all receipts obtained for your fertility treatments for income tax purposes. Please refer to the PCRM Fee Guide for more detail.

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Infertility

What is it?

Infertility is defined as the failure to conceive despite 1 year of unprotected intercourse and affects up to 15% of couples. The cause of infertility can be either male or female factors or a combination of both. Approximately 20% of infertility is unexplained, meaning that the standard fertility workup is normal. Individuals who have been trying to conceive for 1 year, or 6 months if the female partner is ≥ 35 years of age, are encouraged to undergo fertility testing and treatment if indicated.

Folic Acid

Scientific data confirms that folic acid (FA), a common B vitamin, reduces the risk of a serious defects of the central nervous system of the developing fetus, called neural tube defects (NTDs). These conditions include anencephaly, a condition where large portions of the brain, skull and scalp are absent; and spina bifida, which results in malformations of the spinal cord due to a portion of the spinal canal failing to close properly.

The use of FA supplementation, between 0.4 mg and 1.0 mg, has been shown to reduce the risk of problems by 50%. It is recommended that those women who are wishing to become pregnant start taking the supplement during the 2 to 3 months preceding any attempt at conception, and to continue throughout pregnancy. The recommendation from the Society of Obstetricians and Gynecologists of Canada (SOGC) is that women with pregnancies at high-risk for NTDs require increased dietary intake of folate-rich foods (dark green vegetables and pasta) and 5 mg of FA daily. Risk factors include epilepsy, insulin-dependent diabetes, obesity with BMI>35 kg/m^2, family history of NTD, and belonging to a high-risk ethnic group (e.g. Sikh). PregVit© Folic 5 vitamin supplements are available from the PCRM Pharmacy.

Investigations

There are a number of different tests that may be ordered to determine the cause of the infertility and/or best course of treatment. In women, a "day 3" hormone profile to assess ovarian reserve/egg numbers (FSH and estradiol) will be performed, as well as thyroid function testing (TSH), and preconception infectious disease testing. Hormones that affect ovulatory function (prolactin, 17OHP, DHEAS and testosterone) may also be performed depending on your menstrual history. Your physician may also recommend a newer method of assessing ovarian reserve called antimullerian hormone (AMH). To assess the condition and characteristics of your pelvis (including uterus and ovaries) and Fallopian tubes, a pelvic ultrasound, hysterosalpingogram (HSG) or sonohysterogram may be performed. Depending on the results of the initial evaluation, a surgical exploration of the female pelvis or laparoscopy may be indicated, which involves the placement of a fibre optic camera and instruments through small incisions on your abdomen. This procedure provides a more detailed evaluation of the Fallopian tubes and the ability to assess and correct pelvic disorders like adhesion, ovarian masses and endometriosis. Placing a camera through the cervix into the uterus is called hysteroscopy, and commonly performed for the treatment of fibroids, endometrial polyps, uterine septums and intrauterine adhesions. In the male partner, semen analysis is the standard evaluation. Scrotal ultrasound is performed to diagnose an abnormal collection of dilated veins called a varicocele.

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Depending on what information is required by your physician, a sperm test at PCRM may be recommended to provide a more detailed assessment of the sperm.

Counseling Services

The diagnosis of infertility and the methods to treat it are often highly stressful for couples. Counseling services are available through PCRM. For many couples and patients, making the appointment for counseling sessions can be a difficult step. We recommend that patients take the opportunity to utilize this service, to help allay any concerns they may have about their fertility and treatments. For patients who are undergoing IVF treatments, a one hour session is included with the service. For patients undergoing third party reproduction (donor sperm, donor egg), a counseling session is required in accordance with Health Canada regulations. If you have any questions regarding the counseling services, please do not hesitate to ask one of the physicians or nurses for more information.

Healthy Lifestyles

In order to optimize your chances of success with fertility treatments, the physicians at PCRM advocate a healthy lifestyle. This includes the use of prenatal vitamins containing at least 0.4 mg of folic acid, a healthy balanced diet, maintenance of a normal body weight, and physical activity. Patients should refrain from smoking and discuss the use of any medications with their physician.

The PCRM staff recognize the intense anxiety that fertility patients suffer, and do their utmost to minimize stress while under our care. An important part of this is our individualized treatment approach, which includes access to our staff during clinic hours and our PCRM physicians after hours to deal with emergencies and questions. We also encourage a variety of Complementary and Alternative Medicine (CAM) techniques to aid with stress reduction, and potentially enhance the effectiveness of our treatments. Some studies have shown that acupuncture can improve pregnancy rates with in vitro fertilization (IVF) when performed at the time of embryo transfer. Many of our patients also find benefits with the use of yoga and exercise during treatment and throughout pregnancy. Our CAM practitioners are of great value to our patients, by providing not just acupuncture and other interventions, but also a variety of life-style modifications to assist with weight loss and stress relief.

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Treatment Options

Infertility treatment options for women range from simple lifestyle modifications to assisted reproductive technologies like in vitro fertilization (IVF). Both the recommendations of your PCRM physician and the success of treatment will depend on the factors related to your infertility, but in general the treatment course will take a stepwise approach. Your physician might first try ovulation induction, then move to intrauterine insemination (IUI) or superovulation. If none of these procedures are successful, he/she may then recommend more advanced therapies like in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI). To provide a very detailed assessment the genetics of the future baby, a portion of the embryo can now be sampled prior to placing in the uterus. These processes are called Preimplantation Genetic Diagnosis (PGD) and Comprehensive Chromosomal Screening (CCS). These technologies have revolutionized reproductive care by improving pregnancy rates from IVF and reducing the likelihood of miscarriage.

Ovulation Induction

Ovulation induction involves stimulating the ovary to produce one or more eggs in a menstrual cycle. It may be accomplished with a number of different medications and may be helpful in a variety of clinical settings. This treatment may be indicated for women who fail to have ovulatory cycles (anovulation) or very irregular ovulatory cycles (oligo-ovulation). Treatment is typically in the form of oral treatments like clomiphene citrate and letrozole. In women resistant to the effects of these medications, or who have failed to conceive after multiple cycles, superovulation and in vitro fertilization are commonly employed.

Patients with polycystic ovarian syndrome (PCOS) and insulin resistance may also respond to a drug called metformin (Glucophage®). This is a drug that has been used for patients with diabetes for many years. It is safe to be on this medication when trying to get pregnant. The current recommendation is to discontinue its use once pregnancy is confirmed.

Clomiphene Citrate

The most commonly used medication to treat infertility is clomiphene citrate (Serophene® and Clomid®). Clomiphene has been widely used as a first line treatment to induce and augment ovulation. It works within the brain to stimulate the production of gonadotropin releasing hormone, which in turn stimulates the pituitary gland to secrete follicle stimulating hormone (FSH) into the blood stream. FSH, as its name implies, stimulates the development of the ovarian follicles (structures in which eggs reside and mature). Clomiphene is an oral medication that is typically administered for five days starting on either day 3 or 5 of the menstrual cycle. The starting dose is 50 mg per day. If ovulation is not achieved at this dose, the dose can be increased by 50 mg per day until ovulation occurs, or a maximum dose of 200 mg is reached. It may take a couple of months to establish the effective dose.

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Side effects of clomiphene may include abdominal discomfort, hot flashes, vaginal dryness, moodiness, headache and visual disturbances. Whereas most of these side-effects are not harmful, you MUST inform your physician if you experience visual changes, as this is a reason for immediate discontinuation of the medication. Clomiphene is associated with an 8% incidence of multiple births - the vast majority of these being twin pregnancies. A causal relationship between treatment with fertility drugs and ovarian cancer has not been established. The risk of ovarian cancer in clomiphene users, if any, is extremely small.

If clomiphene has not produced a pregnancy within 3-6 cycles, an alternate mode of treatment will be considered. The literature strongly suggests that using clomiphene beyond 6 cycles is unlikely to result in pregnancy.

Letrozole

Letrozole (Femara) is an oral medication belonging to a group of drugs called aromatase inhibitors, which are used primarily for the prevention of breast cancer recurrence. Over the past decade, letrozole has been used as an alternative to clomiphene citrate for ovulation induction. Similar to clomiphene it is easy to use and relatively inexpensive, but has fewer side effects. Letrozole can be used in women with ovulatory disorder, who fail to respond to clomiphene, or those who cannot tolerate the side effects of clomiphene.

Similar to clomiphene, letrozole is used at doses of 2.5 to 7.5mg for 5 days starting on day 3 of the menstrual cycle. It is associated with ovulation rates of over 80% and a thicker uterine lining compared to clomiphene. Letrozole typically stimulates the production of a single egg so multiple pregnancy is uncommon (less than 4%).

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Intrauterine Insemination (IUI)

Intrauterine insemination (IUI) is commonly performed in couples whose infertility investigations have failed to detect a specific cause of infertility (unexplained infertility) or have shown mild male factor infertility. It is also used for therapeutic donor insemination. The procedure involves the placement of prepared ("washed") sperm into the female partner's uterus using a small sterile catheter (fig 1).

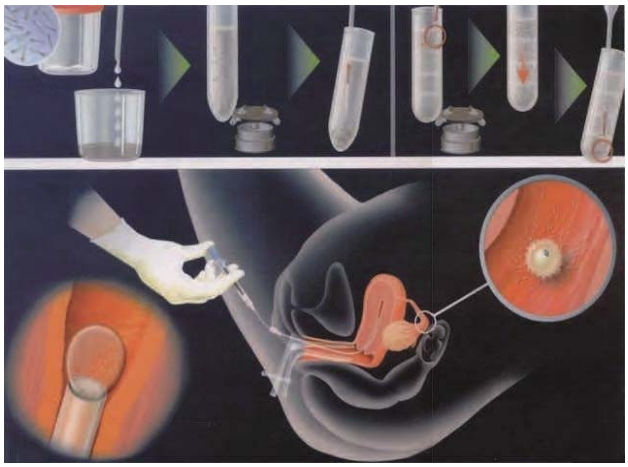
In order for insemination to be successful it must be performed prior to ovulation of the egg. To detect ovulation, urine ovulation predictor kits (OPK) are recommended, which detects the LH surge. These kits are available at PCRM as well as most pharmacies without prescription. Electronic fertility computers/monitors are not recommended while using fertility medication as the higher hormone levels may give a false reading.

The insemination procedure itself requires a visit to the clinic by both partners. During the week, the male partner is required to produce a sperm sample around noon on the day of insemination, with the IUI occurring around 2 pm that afternoon. On weekends and holidays, the sample collection and IUI are performed in the morning. The insemination is typically performed by the nursing staff and is similar to having a Pap test. There is typically little or no discomfort experienced during the IUI procedure.

Generally, an insemination is done each month until pregnancy is achieved or sufficient inseminations have been done to suggest that alternate treatments may be necessary. We will recommend a consultation with your physician after 3-4 inseminations have been completed to evaluate your treatment plan. For various reasons (e.g. vacations, illness) it may not be possible for you to have consecutive inseminations performed. This is not a problem and does not affect your chances of success.

The overall pregnancy rate with superovulation (production of more than one egg) and IUI is 10-20%, with a multiple pregnancy rate of 20-30%. This rate may appear low but is considerably higher than if the couple continued on their own. Your physician will discuss your individual situation and help you to understand your chances for success and treatment options. For couples with infertility, the pregnancy rate with IUI without medication is not higher than simply timing intercourse, so medication will traditionally be recommended.

Figure 1: Intrauterine insemination (IUI)



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Superovulation IUI

Superovulation, or Controlled Ovarian Hyperstimulation (COH), combined with IUI has been demonstrated to be an effective method of treatment for couples where less invasive therapies have not been successful in achieving a pregnancy. The goal of superovulation is to increase both the number of eggs released (3-4 per cycle) to help offset the normal age-related decline in egg quality, that all patients experience to a certain degree. Multiple eggs are generated with the administration of follicle stimulating hormone (FSH), which is the same hormone that the woman's brain naturally produces to make eggs. Given the potential for the production of an excessive number of eggs, patients doing this treatment require close supervision through a fertility centre, to monitor ovarian follicle (contain the eggs) numbers and estradiol levels. Once the follicles have reached the optimum size (18-20 mm), an injection of a hormone called hCG to cause or "trigger" ovulation. HCG is in fact the pregnancy hormone but very similar to the hormone that is naturally released from the brain to cause ovulation. Intrauterine inseminations are typically performed 24 to 36 hours later. HCG is the pregnancy hormone, but structurally very similar to the hormone that causes ovulation naturally, luteinizing hormone (LH). IUI is always recommended when doing superovulation as this has been shown to optimize the likelihood of conception.

The most common side effects with superovulation are lower abdominal fullness and bloating. The most significant risks are high-order multiple pregnancies and ovarian hyperstimulation syndrome. The majority of multiple pregnancies are twins; however, more than two fetuses can sometimes develop. The risk of high-order multiples is actually greater with superovulation cycles compared to IVF, since the number of eggs ovulated cannot be precisely controlled, unlike IVF where eggs are retrieved and a select number of embryos are replaced.

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In Vitro Fertilization (IVF)

In vitro fertilization (IVF) means "fertilization in glass" or the laboratory. It is a sequential process by which one or more eggs (oocytes) are retrieved from the ovary, fertilized in the laboratory with sperm from the male partner and cultured into early embryos. A select number of the resulting embryos are then transferred to the uterus for implantation and pregnancy. There are 6 phases of an IVF cycle: pituitary suppression, ovarian stimulation, egg retrieval, fertilization, embryo transfer and luteal phase support.

Phase 1: Pituitary Suppression

Medications called GnRH agonists (Lupron) and GnRH antagonists (Orgalutran or Cetrotide) are used to inhibit production of the ovulatory hormone luteinizing hormone (LH) from the pituitary gland in the brain, to protect from a "LH surge" and premature ovulation. If a premature LH secretion occurs, the eggs could be lost from the ovary prior to the egg retrieval (ovulation), and the lining of the uterus (endometrium) put "out of phase" relative to the developmental stage of the embryos generated from the cycle, with failure to implant in the uterus.

Phase 2: Ovarian Stimulation

This phase involves the production of multiple ovarian follicles (fluid-filled structures that contain the eggs). In a normal menstrual cycle, the ovaries typically produce a single mature egg. In order to maximize the patient's chance of pregnancy, follicle stimulating hormone (FSH) and luteinizing hormone (LH) are administered by injection to stimulate the production of between 10 and 20 eggs from the ovary. These medications are required for 9-14 days (on average 12). The follicular development is monitored by a series of transvaginal ultrasounds and estradiol (E2) levels (fig 2). Once there are at least 2-3 follicles measuring at least 18mm in diameter, human chorionic gonadotropin (hCG) is given to re-initiate meiotic development within the eggs (clinically referred to as maturation) and loosen the egg complex from the follicle wall to facilitate extraction during the egg retrieval procedure. HCG also serves to stimulate progesterone production from the ovary (corpus luteum generated at each follicle site) and thus provides luteal phase support for the implanting embryo and subsequent pregnancy. HCG is administered by subcutaneous injection 36 hours prior to egg retrieval.

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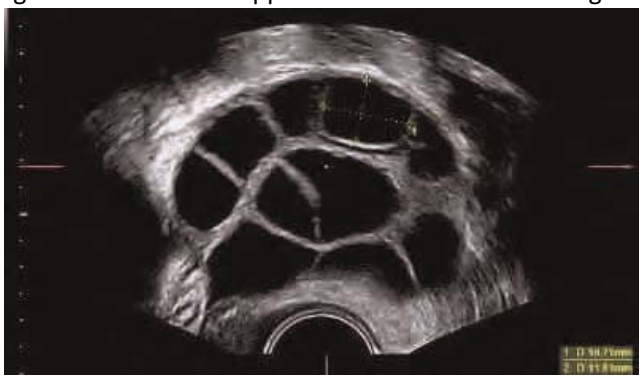
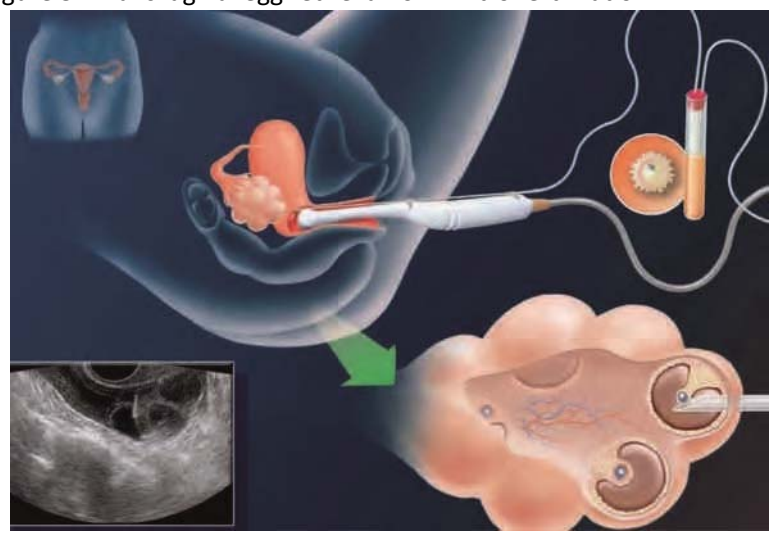
Figure 2: Ultrasound appearance of ovaries following stimulation with follicle stimulating hormone (FSH).



Phase 3: Egg Retrieval

Egg retrieval is an ultrasound-guided needle aspiration procedure to drain the follicular fluid from the ovary (fig 3). Most are performed under conscious (twilight) intravenous sedation using an opioid and benzodiazepine (fentanyl and midazolam). The fluid is then examined under a microscope by the embryology staff. Once eggs are located they are cultured in an incubator until the time of insemination or ICSI approximately 4 hours later, as described below.

Figure 3: Transvaginal egg retrieval for in vitro fertilization.



Phase 4: Fertilization and Embryo Culture

Eggs suitable for fertilization (mature) can undergo the process of fertilization, which starts the afternoon of the egg retrieval. Embryology staff process the semen specimen provided by the male partner or donor and either perform standard IVF insemination by adding approximately 50,000 sperm to eggs in a culture dish, or directly inject the mature eggs with a single sperm through the process of intracytoplasmic sperm injection (ICSI). The eggs are examined the next morning for evidence of fertilization, at which time they are termed zygotes, or a single-cell embryo. Embryos are typically cultured for 3 to 5 days prior to embryo transfer and observed daily to follow their growth and appearance (fig 4). Various methods are used to assess the "quality" of the embryos. At PCRM we use a combination of visual grading under a microscope, and the latest method of following embryo development, time lapse imaging (Embryoscope™). The majority of cases are cultured to the 5th day of development, when the embryo is over 100 cells in size (blastocyst stage). This is the best stage of

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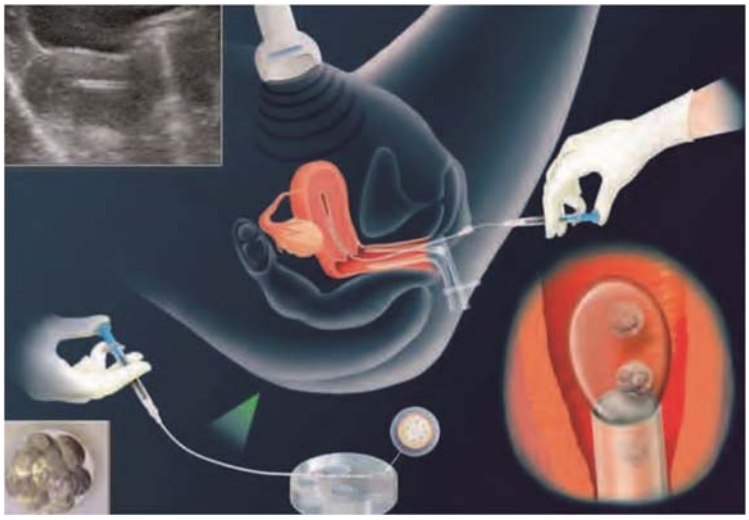
development to select embryos that are most likely to provide for pregnancy, and also the stage that cells can be removed for genetic screening (preimplantation genetic screening/comprehensive chromosomal screening).

Figure 4: Developmental day 3 and day 5 (blastocyst) embryos.

Phase 5: Embryo Transfer

Embryo transfer occurs 3 or 5 days following egg retrieval. Timing of embryo transfer is determined by the number of embryos and their quality. With Preimplantation Genetic Diagnosis (PGD) and Comprehensive Chromosomal Screening (CCS) only embryos that are tested as normal qualify for transfer. The number of embryos transferred is based on several patient specific considerations including age of female partner, quality of embryos, past fertility history, and very importantly, the implantation rate (probability of each embryo developing in the uterus) of the particular clinic. The patient is requested to have a full bladder so that transfer may be visualized using ultrasound guidance and also helps straighten the uterus in patients with an anteversion (80% of women). The embryos are loaded into a soft, flexible catheter attached to a syringe and passed through the cervix into the uterus (fig 5). Gentle pressure is then applied to the catheter syringe and the embryos are released into the uterus.

Figure 5: Ultrasound-guided embryo transfer.



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Phase 6: Luteal Phase Support

The IVF process requires the supplementation of progesterone to support the endometrial lining at the time of implantation and early pregnancy. Following the pituitary gland suppression that is required for treatments like IVF, endogenous production of progesterone can be inadequate and result in a luteal support deficiency and pregnancy loss. As mentioned previously, hCG stimulates progesterone production from the ovaries, and combined with a long half-life (48 hours) in the circulation, provides for an excellent form of luteal phase support. Progesterone supplementation is most commonly given as either vaginal suppositories or intramuscular injection.

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Embryo Cryopreservation

Approximately 30-50% of couples undergoing IVF will have surplus embryos after completion of the embryo transfer procedure. The recommendation is to cryopreserve these embryos for transfer in a future cycle, in the event of a failed fresh attempt or after completion of pregnancy. Greater than 90% of embryos should survive the freeze/thaw process and pregnancy rates are generally at least 10% lower than those of a fresh cycle.

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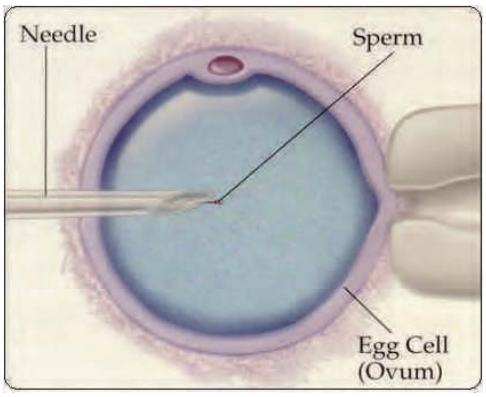
Intracytoplasmic Sperm Injection (ICSI)

Male factor infertility is present in up to half of all infertile couples, making it one of the most common causes of infertility. In the past, the only option for many male factor couples was intrauterine insemination (IUI) using donated sperm. Intracytoplasmic Sperm Injection (ICSI) is performed as a part of an IVF cycle wherein a single sperm is inserted directly into the egg causing fertilization. The ICSI procedure does not appear to damage the egg and optimizes fertilization rates in cases where a male factor exists. ICSI was a major advance in the treatment of male infertility, allowing virtually all men to father children, with the first case performed in 1990.

The decision to use ICSI is made in consultation with the couple, physician, and embryologists. At most fertility clinics this decision is made based on the sperm testing at the clinic. However, there are some instances where the semen sample collected at the time of retrieval is not optimal, and ICSI may be recommended at that time. ICSI is performed on the day of egg (oocyte) retrieval. A sperm sample is provided by the partner, and approximately 4-6 hours after the egg retrieval, individual sperm from this sample is injected into the mature eggs (fig 5). Fertilization rates with ICSI are typically about 80% of mature (competent) eggs. Of note, standard IVF insemination of eggs should yield the same fertilization rates, but is reserved for cases when the sperm is considered normal and there is no history of poor fertilization with IVF in the past.

Figure 5: Intracytoplasmic sperm injection (ICSI).



Many times the sperm needed for ICSI are retrieved from the ejaculate; however, men with no sperm can often still produce sperm for ICSI. The sperm can be retrieved directly from the testicles using testicular sperm extraction (TESE) or from the epididymis using percutaneous epididymal sperm aspiration (PESA). Fertilization rates using ICSI are typically high, and pregnancy success rates are higher compared to standard IVF culture when a sperm factor is the cause of infertility.

PCRM pioneered a surgical procedure in Canada called microsurgical testicular sperm extraction (microTESE), for men with a complete absence of sperm (azospermia). This is possible because of our unique ability to provide reproductive surgery under general anesthesia (as a level 1 surgical centre). In these cases only small numbers of sperm are available from the testicular surgery, such that freezing cannot effectively be performed for future treatments. This fresh sperm is then used to fertilize fresh eggs that have been collected from an IVF cycle which has been synchronized with the microTESE procedure.

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Pharmacy

PCRM is pleased to offer an on-site licensed pharmacy. The PCRM Pharmacy provides a wide range of fertility and hormonal medications at competitive rates. For our clients outside of Edmonton, we also provide a convenient Canada-wide shipping service. PCRM is a provider for the following insurance carriers and the insurance companies that they administer: ESI Canada, Green Shield Canada, Pacific Blue Cross, Alberta Blue Cross, First Canadian Insurance, Claim Secure and NexgenRx. As a provider for these companies we are able to adjudicate claims electronically at the time the medications are dispensed. Our pharmacy staff are not authorized to access your personal insurance information, so would never interface with your insurer directly without your permission. Signing of an Insurance Investigation Consent will allow one of our pharmacy technicians to contact your insurer. However it is your responsibility as the patient to know your fertility drug coverage in advance of treatment and whether pre-authorization is required. We have listed all of the fertility medications prescribed at PCRM on the next page to assist with this process. Your insurer may ask for specific drug identification numbers (DIN) in order to process your request. Our physicians will gladly provide you with a letter in defense of your coverage. An official pharmacy receipt is always generated with your prescription that can be submitted manually to your insurer for reimbursement in the event that the electronic submission is denied. Also, depending on your particular policy and insurer's reimbursement structure, a balance may be due after the adjudication is successfully completed.

As stated in the Alberta College of Pharmacists guidelines, PCRM cannot re-circulate medication that is returned by patients. Our staff will do their utmost to prescribe the minimum amount of medication needed to complete your treatment. Despite this, you may find yourself with excess medication after completion of the cycle if your medication requirements are lower than expected. If stored correctly, most of the medications will not lose potency for months to years, so can be safely used for future treatments, in the event that the current treatment is unsuccessful. We cannot accept returns, however all orders erroneously dispensed will be reimbursed or refilled correctly.

Our medical staff has extensive experience with fertility medications, and is available 24/7 to provide support while under our care.

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Drug Identification Numbers (DIN'S)

Drug		DIN
GnRH Agonist	Lupron 5mg/ml 2 wk kit	00727695
	Depot Lupron 3.75 mg injection	00884502
GnRH Antagonists	Cetrotide 0.25 mg injection	02247766
	Orgalutran 0.25 mg injection	02245641
Gonadotropins	Gonal F Pen 300IU	02270404
	Gonal F Pen 450IU	02270390
	Gonal F Pen 900IU	02270382
	Puregon Pen/cartridge 300IU	02243948
	Puregon Pen/cartridge 600IU	02243948
	Puregon Pen/cartridge 900IU	02243948
	Luveris 75IU	02269066
	Bravelle 75IU	02268140
	Menopur 75IU	02283093
HCG	Human Chorionic Gonadotropin 10,000 IU	02247459
	Pregnyl 10,000 IU	02182904
	Ovidrel Syringes 250 mcg	02262088
	Ovidrel Pen 250 mcg	02371588
Progesterone	Prometrium 100 mg capsules (box 30)	02166704
	Endometrin 100 mg vaginal tablet (box 21)	02334992
	Crinone 8% gel 90 mg (18 appl)	02241013
	Progesterone in Oil injection 50 mg/ml (10ml)	01977652
Miscellaneous	Estrace 2 mg (bottle of 100)	02148595
	Apri 21 day	02317192
	Clomiphene Citrate (Serophene, Clomid) 50mg	00893722
	Letrozole (Femara) 2.5 mg	02343657
Prenatal Vitamins	Pregvit Pregvit Folic 5	02246067 02276194

The Drug Identification Number (DIN) is used by insurance companies to identify the drugs submitted in a claim. To find out whether your drug plan will cover these drugs, contact your benefit provider and provide them with the above DIN's.

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Ovarian Hyperstimulation Syndrome (OHSS)

Ovarian hyperstimulation syndrome (OHSS) is a complication related to the stimulation of ovaries with IVF. The condition is most commonly encountered during the luteal phase of the treatment and early into the resulting pregnancy. It is associated with enlarged ovaries, high hormone levels and accumulation of fluid in the abdomen (ascites). A variety of IVF stimulation protocols can now virtually eliminate the risk of this condition.

Mild Ovarian Hyperstimulation

Symptoms include: abdominal bloating, a feeling of fullness, nausea, diarrhea, and weight gain.

What Should You Do?

- Weigh yourself at approximately the same time each day.
- Refrain from intercourse for approximately 4 weeks or until pregnancy test results are known.
- Avoid vigorous activity, heavy lifting or straining.
- Keep yourself comfortable by avoiding tight fitting clothing and taking Tylenol for any discomfort.
- Maintain normal nutrition, including adequate fluid intake.

Moderate Ovarian Hyperstimulation

Symptoms include: weight gain of more than 2 pounds over 24 hours, distended abdomen, nausea and vomiting, occasional shortness of breath (typically while lying flat).

What Should You Do?

- Call the clinic and speak with a nurse.
- Weigh yourself at about the same time daily.
- Keep a rough record of your fluid intake and how much urine you are passing.
- High sodium diet replacement is the best oral fluid replacement (Chicken noodle soup or vegetable drinks like V8). Sports drinks like Gatorade® and PowerAide® also contain sodium but in low amounts and contain too much sugar and water.
- You should be examined by a PCRM physician.
- Keep yourself comfortable by avoiding tight fitting clothing and taking Tylenol for any discomfort.

Severe Ovarian Hyperstimulation

Symptoms include those listed for mild and moderate plus: shortness of breath, low urine output, severe abdominal bloating, pain in the lower abdomen, and coughing.

What Should You Do?

CALL THE CLINIC IMMEDIATELY.

- You will likely be asked to return to the clinic for assessment and to have the fluid in the abdomen removed via a procedure called paracentesis. You may also require hospitalization and intravenous fluid therapy.

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Common Fertility Medications

Many medications are used in IVF to help promote follicular growth and endometrium development. They work together to increase the number of developing follicles, control the timing of ovulation and prepare the endometrium for implantation.

Birth Control Pill preparation	Oral tablets used to help prime the ovaries for IVF and help to regulate menstrual cycles.
Estrogen (Estrace)	Oral tablets used to prepare the endometrium for implantation during a cryopreservation cycle.
GnRH agonists (Lupron)	Injectable medication used in the pituitary suppression stage of IVF. It is used to "switch off" your own hormone system and prevent ovulation.
GnRH antagonists (Orgalutran, Cetrotide)	Block the effects of LH which helps prevent ovulation from occurring prior to egg retrieval.
Gonadotropins (Puregon, Gonal-f, Menopur, Bravelle)	Injectable medications containing FSH that is necessary for the recruitment, growth and maturation of follicles within the ovaries.
Human Chorionic Gonadotropin (PPC, Ovidrel)	Injectable medication given prior to egg retrieval to help with the final maturation process and prepare the follicles for ovulation.
Metformin	Oral medication used on women with polycystic ovarian syndrome (PCOS) and/or elevated insulin levels and used to bring on ovulation.
Progesterone (Prometrium, Endometrin, Progesterone in Oil)	Used in the final phase of IVF to maintain the endometrial lining and support an early pregnancy.

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Recommended Websites

pacificfertility.ca

Fertility Patient Resources

www.assistedconception.net

The Assisted Conception Taskforce (ACT) is an international group of patient leaders and health professionals from 20 countries with interest and expertise in the difficulties of conceiving.

www.fertilitylifelines.com

Serono Canada Inc. patient resource site

www.myfertility.ca

Merck Canada Ltd. patient resource site

www.ferringfertility.ca

Ferring Fertility Canada patient resource site

Society Websites

www.cfas.ca

Canadian Fertility and Andrology Society (CFAS)

www.asrm.com

American Society of Reproductive Medicine (ASRM)

Early Prenatal Screening

www.mfmedicine.com

Great resource for 1st trimester screening and fetal ultrasound

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Glossary of Terms

A diagnosis of infertility is stressful and can take couples on a roller coaster ride of new information and learning. We have compiled a list of commonly used terms along with their meanings that we hope will aid with the process of managing your infertility.

Andrology: The study of male reproduction

Anovulatory Bleeding: The type of menstruation often associated with failure to ovulate – may be scanty and of short duration or abnormally heavy and in irregular patterns

Artificial Insemination: A procedure by which a sperm from the male partner is prepared and placed either in the cervix or high in the uterus of the female partner

Azoospermia: The absence of sperm

Clomiphene Citrate: synthetic drug used to stimulate the hypothalamus and pituitary gland to increase FSH and LH production

Corpus Luteum: The special gland that forms in the ovary at the site of the released egg. This gland produces the hormone progesterone during the second half of the normal menstrual cycle

Cryopreservation: A procedure used to preserve (by freezing) and store embryos or gametes (sperm, oocytes)

Dysmenorrhoea: Painful menstruation

Ectopic pregnancy: The development of a fertilized egg outside the womb; embryos may migrate into the fallopian tube and lodge there rather than returning to the uterine cavity for normal development

Embryo: The term used to describe the early stages of fetal growth, from conception to the eighth week of pregnancy

Embryo transfer: Introduction of an embryo into a woman's uterus using a small catheter

Endometriosis: The presence of endometrial tissue (normal uterine lining) in abnormal locations such as the tubes, ovaries and peritoneal cavity, often causing infertility and painful menstruation

Endometrium: The lining (endometrial tissue) that builds up inside the uterus

Epididymis: The coiled tube attached to the back and upper side of the testicle that stores sperm and is connected to the vas deferens

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Estradiol: A hormone released by developing follicles in the ovary. Plasma estradiol levels are used to help determine progressive growth of the follicle during ovulation induction

Estrogen: A class of female hormones produced mainly by the ovaries from the onset of puberty and continuing until menopause and which are responsible for the development of secondary sexual characteristics

Fallopian tubes: A pair of narrow tubes that carry the ovum (egg) from the ovary to the uterus

Fertilization: The penetration of the egg by the sperm and fusion of genetic materials to result in the development of the embryo

Fibroid: A mass of fibrous tissue that may occur in the uterine wall; may be totally without symptoms or may cause abnormal menstrual patterns or infertility

Follicle stimulating hormone (FSH): At the beginning of each cycle (ovulation) the ovaries receive this hormonal signal that stimulates the follicles to grow and develop

Hormone: A chemical, produced by an endocrine gland, which circulates in the blood and has widespread action throughout the body

Hypogonadotropic hypogonadism: A state of complete failure to produce gonadotropins that can be brought about by surgery or radiotherapy for a pituitary tumour, and is found in some women who are severely underweight such as some female marathon runners

Hypothalamus: The part of the central nervous system (central area on the underside of the brain) that communicates with the pituitary gland to control involuntary functions such as body temperature and the release of hormones

Implantation: The embedding of the fertilized egg in the endometrium of the uterus

Infertility: The inability to conceive after repeated intercourse without contraception for one year

Intracytoplasmic Sperm Injection (ICSI): A procedure which involves the injection of a single sperm into an egg to increase the chances of fertilization

In Vitro Fertilization (IVF): A procedure in which several eggs are retrieved from the ovary, fertilized in the laboratory with sperm from the male partner, and a small selection of the resulting embryos are then transferred to the womb for transplantation

Laparoscopy: The direct visualization of the ovaries and the exterior of the fallopian tubes and uterus by means of inserting a surgical instrument through a small incision below the navel

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Luteal Phase: The days of the menstrual cycle following ovulation and ending with menses during which progesterone is produced

Luteal Phase Defect: A shortened luteal phase or one with inadequate progesterone production

Luteinizing Hormone (LH): A hormone secreted by the anterior lobe of the pituitary throughout the menstrual cycle; secretion of LH increases in the middle of the cycle to induce release of the egg

Oligozoospermia: Too few sperm

Ovarian Failure: The inability of the ovary to respond to any gonadotropic hormone stimulation, usually due to the absence of follicular tissue on a genetic basis or the postmenopausal condition

Ovarian Hyperstimulation Syndrome: A syndrome that may include ovarian enlargement, gastrointestinal symptoms, abdominal distension and weight gain. Severe cases may be further complicated with cardiovascular, pulmonary and electrolyte disturbances, requiring hospitalization

Ovary: The sexual gland of the female which produces the hormones estrogen and progesterone. There are 2 ovaries, one on each side of the pelvis which are attached to the uterus by the fallopian tubes

Ovulation: The release of a mature egg from the ovary, usually at about the midpoint of the menstrual cycle

Ovulation Induction: Drug treatment that stimulates the ovaries to produce a single mature follicle to induce ovulation

Ovum: The egg cell produced in the ovaries each month

Pituitary: A gland located at the base of the human brain that secretes a number of important hormones related to normal growth and development of fertility

Polycystic Ovarian Syndrome (PCOS): Development of multiple cysts in the ovaries due to arrested follicular growth, resulting in an imbalance in the amount of LH and FSH released during the ovulatory cycle

Progesterone: A hormone secreted by the corpus luteum of the ovary after ovulation has occurred; also produced by the placenta during pregnancy

Semen: The thick white fluid released during ejaculation

Sperm: A male gamete or reproductive cell; a spermatozoan

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Testosterone: The most potent male sex hormone, produced in the testicles. It is also produced in much lower amounts in the female ovary

Varicocele: Varicose (enlarged) veins around the testicles that is associated with male factor infertility

Vas deferens: A pair of ducts that carry sperm from the testes to the urethra during ejaculation. Contraction of its thick muscular wall propels sperm rapidly through the duct, which forms part of the spermatic cord

Zona pellucid: Shell around the egg

Zygote: An ovum that has been fertilized by a sperm

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