Male Infertility

Southern Ontario
Fertility Technologies

Definition

Male infertility is said to occur when a couple is unable to conceive after **one year of trying** and there is an indication from history, physical examination, semen analysis or more involved tests of sperm function that there is an **abnormality with the semen.**

Frequency

One in 6 or 7 couples will seek medical advice because of delay in getting pregnant. Of these couples, **30% will be due to male factor alone and male factor will be a contributor in another 20%**. It is our impression that the incidence of male factor infertility is higher in Southwestern Ontario than in other areas of the country. We do not know the reason for this but one wonders if environmental toxins, dietary factors or lifestyle factors are to blame.

Semen Analysis

The mainstay of determining if male infertility is present is a semen analysis. This involves the collection and examining of the fluid ejaculated from the penis at the time of climax. Two semen analyses are usually requested for an infertility investigation. This is because semen samples vary widely. **The same male may produce samples, which vary 1,000%!** Sometimes an abnormality will be apparent on one sample but not the other.

A normal semen analysis should have a volume of at least 1.5 ml, and a concentration of at least 20 million sperm per ml of fluid. At least 50% of the sperm should be moving and at least 30% should appear normally formed. Sperm morphology (are the sperm normal in appearance?) is the least predictive of the values and the hardest to determine, especially in labs were the technicians may not be used to evaluating sperm morphology. We also like to see a total of 40 million moving sperm in the total ejaculate. These guidelines are from the **World Health Organization** and serve as a good screening test to alert us to the possibility of male factor infertility. However, a normal semen analysis does not mean that there isn't a problem and spontaneous pregnancies can occur with abnormal sperm tests.

Parameter	Normal Level
Volume	1.5 ml or greater
Concentration	20 million sperm / ml or greater
% Motility	50% or greater
% Normal Appearance	30% or greater
Total Motile Count	40 million sperm or greater

Sperm quality does decrease with age but the male's age is not nearly as critical as female age. The following chart illustrates what % of sperm expected to be abnormal at different male ages. There is no evidence that increased abnormal sperm result in increased congenital abnormalities.

Age	% Abnormal
22	25
30	40
40	60
60	85

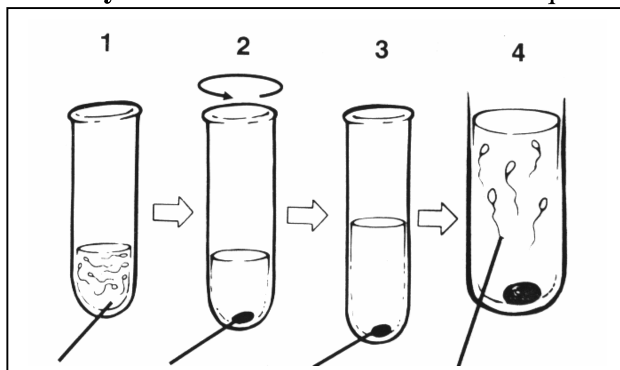
The Semen Sample Collection

Many commercial labs or hospital labs will perform semen analysis, however it is **best to call the lab** intend using before taking the sample in. We will also perform semen analysis at S.O.F.T. The sample should be produced after **two days** with no ejaculation. Longer periods of abstention are not necessary. The ejaculate should be produced by **masturbation** and collected directly into the container provided. Many men have difficulty with this. Your partner can help you with masturbation. If you find this impossible, you cannot ejaculate into a condom and empty this into the container. Condoms contain spermacides (substances that kill sperm) and this may give false results. If you feel you will have a great deal of difficulty with this you should discuss this with your infertility physician, as special non-spermicidal condoms and counseling are available.

Many labs will have a room available on-site for you to produce your sample. A **"men's room" is available for this purpose at S.O.F.T.** If you find it uncomfortable or inconvenient, your specimen should be taken to the lab as quickly as you can. It was said that a semen sample had to be delivered to the lab within an hour. We now believe this is not as critical as it was once thought. It is important when transporting your sample to the lab to keep it **between room and body temperature**. In the winter this is most easily done be carrying it next to the body under a shirt or sweater. It is probably good to transport it this way even in summer months as this insures that it is kept out of the sun. Many of our couples from up to two hours away will still produce their sample at home and drive it to us. Many times we can examine a semen sample up to 24 hours after it has been produced and find it is still in good condition. If a semen sample is produced in the comfort of ones own home it may be of much higher count than if it is produced on the lab site. Only sometimes when we feel there may be a severe problem with the semen or it does not seem to transport well, will we ask you to produce it on site.

Sperm Function Testing

In addition to the usual semen analysis, the function of the semen sample is usually evaluated if there is a suspicion of male factor infertility or prior to starting IUI or IVF. This test is called a **"Monash" semen analysis**. "Monash" refers to a technique to measure the ability of the sperm to swim. The test involves the following steps … (1)The sperm sample is suspended in media. Media is a solution of salt and protein, which is very similar to the fluid found in the fallopian tube. Then the sperm are (2) spun down into a pellet. (3) Fresh media is then suspended over the pellet of sperm. (4) The sperm in the pellet are then incubated (let stand at body temperature) and good ones will swim up into the media. The number of sperm that swim up into the media indicates how many functional sperm are in the sample.



When the "Monash" is done we also include preparing the semen in several ways to determine how to obtain the highest sperm count for insemination. There are several recovery techniques used to "wash" sperm for intrauterine insemination. We try to determine which recovery technique works best for your sample. This is important because the more sperm that can be inseminated, the more likely a pregnancy will occur.

The "Monash" is not covered by OHIP and we charge you **$100.00** to cover the lab expenses. At S.O.F.T. the "Monash" is usually performed with the first insemination and is incorporated in the first sperm wash fee in order to save you money.

The Psychology of Male Factor Infertility

Males react very differently to infertility than females. Females feel loss and sadness but are able to discuss this and share it with people around them. Males however, find it difficult to share their feelings with others. Their immediate reaction is to not deal with it. They may rationalize it by thinking that children are not as important to their lives as they originally thought. It is not discussed.

However, the knowledge of the male factor can express itself later in **depression**. The depression is not always consciously linked to infertility. They can also develop feelings of **inadequacy and decreased self worth**. Many men also feel **guilty** in that they cannot provide their partner with a baby. The best thing is of course to talk about it. Remembering that infertility is a couple's issue and usually there is some sub-fertility factors in both members of the couple. It is helpful to ask the man the following question – "If your wife had endometriosis and couldn't get pregnant, would you blame her?" The answer is always "no". Then you shouldn't blame yourself for having a low sperm count!

Causes of Male Factor Infertility

The male partner of a couple may have a low sperm count for many reasons. However **in the vast majority of men in this situation no cause is apparent.** This is often referred to as idiopathic male factor infertility.

Sperm counts can be low or absent because the testicles are not making many sperm or because there is a blockage or partial blockage to the sperm getting from the testicle into the ejaculate.

Low sperm production can be caused by genetic (inherited) problems and developmental problems (difficulties when the testicles

were first forming). Hormone deficiencies can cause decreased sperm counts but this is relatively rare and usually apparent from physical examination. Infections, trauma and toxins can all caused decreased sperm counts. Previous surgery, radiation or chemotherapy can be detrimental.

Infectious causes of male factor infertility are rare but chronic prostatitis can probably cause inflammation in the prostatic fluids that makes up a large part of the ejaculate. Diagnosis of this can sometimes be suspected from history or physical examination. Often, many white cells (puss cells) are found in the semen. Treatment of this can sometimes involve the long-term use of antibiotics. Sometimes, when this appears to be a problem, we will have the male ejaculate directly into some media to try and reduce the exposure of the sperm to the prostatic fluid. There is however, no proof that this is beneficial. Some physicians promote the use of broad-spectrum antibiotics for all men and women with infertility. There is no proof for this and some harm may come from it.

Varicocoeles (varicose veins of the scrotum) can also cause decreased sperm count and motility. Varicocoelectomy (surgical removal) or embolization of the abnormal veins can result in an improvement in these parameters but has not by been proven to increase the chance of a pregnancy. A Varicocoelectomy is not always indicated even when a low sperm count and a Varicocoeles is found. An example is if the count is so low that doubling or tripling the count will not improve the chances of pregnancy with a certain technology (I.E. – IUI) then there is no point in doing it.

Lower sperm counts may also result from **life style factors** such as decreased frequency of ejaculation, inactivity or poor diet. Factors often sited to cause low sperm count such as tight underwear, saunas, hot tubs and alcohol (in moderation) probably have no effect. Cigarette smoking is a negative fertility factor for both males and females. Chronic illnesses may also cause decreased sperm counts.

Obstruction of the ducts from the testicle can be associated with being a carrier of the cystic fibrosis gene, infection, previous surgery or trauma. Unfortunately, reconstruction of the ducts is not usually possible but retrieval of sperm from the testicle is usually very successful. Sperm retrieved from the testicle or epididymis cannot fertilize the egg and therefore must be used with intracytoplasmic sperm injection.

Retrograde Ejaculation

Male factor infertility may also exist because of retrograde ejaculation. This occurs when climax occurs but the semen is ejaculated into the bladder instead of forward out of the penis. It can be caused by abnormalities in development of the base of the bladder, injuries or surgery in this area or by diseases that affect the nerves in this area. Diabetes is one of the more common conditions that can do this.

This can usually be treated successfully. The woman’s cycle is monitored to determine precisely when ovulation will occur. The man takes sodium bicarbonate by mouth to prevent the urine from being too acidic. The bladder is emptied completely and media is placed into the bladder using a fine catheter. The man then ejaculates and the urine is collected. The sperm can be isolated from the urine, re-suspended in fresh media and used for intrauterine insemination.

Spinal Cord Injuries

Often after a severe injury to the spinal cord, ejaculation is no longer possible. In this situation, ejaculation can by caused by stimulating the prostate area, through the rectum with an electric current or vibration.

When ejaculation occurs under these circumstances, it is mostly retrograde into the bladder. However this can be retrieved using the techniques described above with retrograde ejaculation. Semen collected in this way can then be used for insemination or IVF.

The Interaction of Male and Female Infertility Factors

Approximately 7% of females and **5% of males** will have some factor that decreases their ability to become pregnant. If these sub-fertile individuals coupled randomly, you would expect less than 1% of couples to have a problem with both the male and female. However, **when couples are evaluated for infertility, 20-30% of couples are found to have sub-fertility factors in both members**. The reason is a very fertile female will compensate for a less fertile male and this couple never presents for evaluation. Similarly, a very fertile male may compensate for a less fertile female. However, a female with mild female-factor infertility may unmask a male with mild male-factor infertility. Similarity, a male with a lower sperm count may unmask a female partner with mild infertility factors.

If a man has a low sperm count but it is not zero, the woman is more likely to have a sub-fertility factor.

Treatments for Male Factor Infertility

1) Medications and Lifestyle Changes

Giving up **smoking** is an excellent idea not only because it improves fertility but because it improves health in general.

No medications or lifestyle changes have been proven to help improve sperm counts. However, several things may help and will be discussed here.

Vitamin **C and E** as well as **zinc and folic acid** may be beneficial for maintaining sperm counts and may improve them. These can be obtained in a good multivitamin with minerals. Usually we suggest a double dose. A recent study reported in one of our main infertility journals, was able to demonstrate an improvement in sperm counts with supplemental zinc and folic acid in the diet.

It has been observed in animals that a fatty acid called **DHA** (docosahexaenoic acid) is found in higher concentrations in semen samples with a high total motile count. DHA's claim to fame is that it is present in the fish oils that appear to protect the Eskimos from heart disease even though they eat a diet very high in whale blubber. Several epidemiological investigations have indicated that long-term consumption of fish appears to be associated with a decreased incident of heart attacks.

In the past, I was involved in two studies involving DHA and sperm counts. The first study looked for a similar correlation in humans between DHA concentration in the semen and sperm count as was found in animal semen. The same relationship exists in humans; the higher the sperm count, the higher the concentration of DHA in the semen

The S.O.F.T. "Potion" for Male Factor Infertility

1) **Multivitamin with Minerals Twice a Day (Vit C, Vit E, Zinc, and Folic Acid)**
2) **Salmon Oil Capsules (DHA) Two or Three Times A Day**
3) **Increased Frequency of Ejaculation**
4) **L-carnitine 330 mg Three Times Per Day**
5) **Diet and Exercise To Promote General Health**

In the second study, we attempted to demonstrate an improvement in sperm counts with supplementation of DHA in the diet. In that study we were unable to prove an improvement in the total number of moving sperm improved with dietary supplementation of DHA because of the extreme variability between semen samples in the same man and the low sample size (only 20 couples in each group). However, in the six months of the trial, 3 couples in the DHA group attained a pregnancy and none did in the placebo group.

In the United States a none-essential amino acid called **L-carnitine** is used widely to promote sperm motility. In the past a similar amino acid, L-arginine has also been used but is seldom used today. Several scientific studies have indicated its usefulness. Very recently, a report proved its usefulness in men with chronic low-grade infection of the genital tract. However, at S.O.F.T. we are very convinced that it is useful in almost all men with low sperm counts. Our lab director has observed not only an increase in the percent motility but also an increase in the quality of the sperm motion.

There has been debate and it is controversial, but many observations have indicated a general decrease in male sperm counts over the last 60 years. No one knows what may have caused this, however, if it is a real observation, it is intriguing to speculate that this may be caused by deficiencies in the diet. In the next year, S.O.F.T. will be running a clinic trial to try to prove some of these nutritional agents improve sperm counts. You may be asked to take part in this study.

The additives mentioned we refer to as **the "S.O.F.T. Potion"**. We have been suggesting it for three years. We have observed the majority of men to improve their counts. The improvement occurs slowly. The sperm cycle (the time it takes to make a sperm) is 72 days. We usually don't see an improvement for three months and can continue to see improvements for up to one year.

Sexual Frequency

It is commonly said that when you are trying to get pregnant, you should only have intercourse every other day to maintain a high sperm count. **This is absolutely incorrect!!!** It is true that when we are doing intrauterine insemination that we ask you to refrain from intercourse for 2 days before the insemination. However, this is because you are ejaculating into a bottle and we want the insemination count to be as high as possible. It is also because with semen analysis, we need to standardize it so to be able to compare counts. However, if ejaculation occurs into the vagina, each ejaculation adds additional sperm. For example, if sexual intercourse were to occur in the morning it may contain 100 million sperm. If later that same day, intercourse were to occur again, there may only be 75 million sperm. However, that means there are 175 million sperm in the vagina.

Also, there was a large study that looked at environmental factors and sperm counts. It examined tight underwear, cigarettes, alcohol, coffee, saunas, hot tubs and other

environmental factors. None of them were found to correlate! However, what the study did find is that men who tended to ejaculate more often tended to have higher sperm counts. For example, a man who had sexual intercourse 2 to 4 times a month would usually have a much lower sperm count than a man who had intercourse 20 times a month. We therefore will usually advise couples who are experiencing infertility to increase their frequency of intercourse or at least ejaculation.

There are also several studies that demonstrate that the time from trying to get pregnant to achieving a pregnancy is indirectly proportional to the frequency of sexual intercourse. This has been demonstrated both with spontaneous pregnancies and with infertility treatment.

2) Surgery

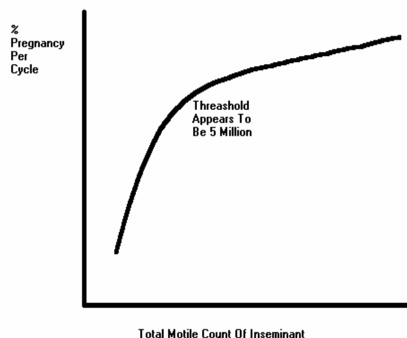
Varicocoeles are believed to decrease sperm quality by decreasing both the count and especially the concentration. Varicocoeles can be removed surgically or can be treated by embolization.

Non- descended testicles are usually corrected in young boys. Men with a history of this surgery will often have low sperm counts. It is thought that not only does the non-descention of the testicle adversely affect the sperm count but testicles which do not descend may be more commonly abnormal.

Other surgical procedures may be beneficial in some circumstances. **Reanastomosis** is possible after vasectomy and with congenital blockage. **Sperm retrieval** is a useful procedure and is discussed in more detail later.

3) Intrauterine Insemination

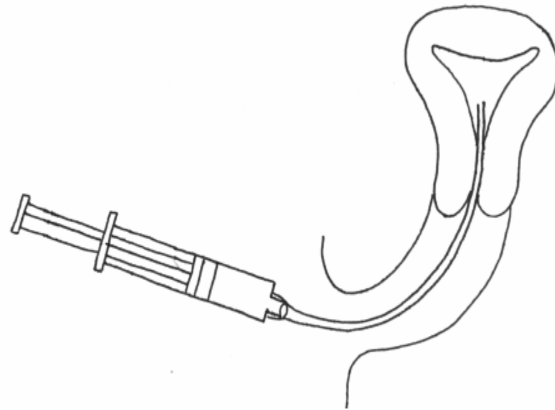
Once a diagnosis of male factor infertility is made several treatment options are available depending on the severity of the problem. For less severe forms, were count, motility or morphology is decreased from expected levels, **sperm washing and intrauterine insemination (IUI)** may be an option. We believe IUI helps with mild to moderate male factor infertility because it improves the number of sperm available in the uterine cavity. The success of intrauterine insemination with male factor infertility depends on the number of motile sperm, which can be recovered in the washed semen sample. Experience with this technique as well as from the medical literature suggests that recovery of 2 million



It is generally believed that 3-5% of the sperm ejaculated into the vagina are able to navigate the cervical mucous and end up in the uterine cavity. Usually when the sperm is washed, we can recover 30-50% of the moving sperm and place these in the uterine cavity.

or less sperm gives a pregnancy rate of 3.5%. Although this seems very low, the chance of a spontaneous pregnancy in these circumstances is probably close to zero. Recovery of 2 to 6 million sperm gives a pregnancy rate of 6 to 7% per cycle and recovery of more than 7 million sperm gives pregnancy rates of up to 15%. A threshold seems to occur, were once 5 million sperm can be isolated, that everybody's chance is about equal (see graph). Generally, we would prefer to do inseminations with 5 million sperm or more. However we feel that intrauterine insemination is worth doing for couples as long as 1 million sperm can be recovered. Although the pregnancy rate at this level is not as high, is still improves the chance over intercourse alone A pregnancy has occurred at a sperm recovery of 0.16 million. If below 1 million sperm are recovered, intrauterine insemination may be postponed while we try with the "S.O.F.T. potion" to improve the sperm count or IVF with ICSI may be recommended.

Intrauterine insemination is the deposition of sperm into the cavity of the uterus using a fine plastic catheter at the time of ovulation. Before semen can be injected into the uterine cavity it must be "washed". **"Sperm washing"** is the process of separating the sperm from the rest of the seminal fluid that makes up 95% of the volume of the ejaculate. This is done in the lab. Several techniques are available and the one that produces the highest sperm count will be chosen for you. This process is not covered by OHIP and you will be **charged $200.00.** This makes IUI a very affordable treatment for most couples.



Intrauterine insemination is usually combined with some form of stimulation for the female partner. This may be as simple as clomiphene citrate or can be as complicated as a full IVF-type stimulation protocol. Information sheets are available for S.O.F.T. covering the different stimulation protocols.

Intrauterine insemination cycles involve careful monitoring of the cycle so that the insemination can be done at the time of ovulation. Some controversy exists as to whether two inseminations may improve the chance of a pregnancy over one. Last year we completed a large clinical trial at S.O.F.T. to try and settle this question. The trial indicated that in general, two inseminations do not give superior results over one insemination. However, in the subgroups were there is male factor present (defined as a sperm recovery of less than 5 million) and when insemination was timed by a spontaneous LH surge rather than giving an HCG injection, there was an improvement. In fact, if both of these factors were present, the improvement in pregnancy rate was almost 5%. A double insemination is available at S.O.F.T. for $225.00.

2) Donor Insemination

Having a baby through donor insemination usually does not involve complex medical technology but does require you to make some very important decisions

that aren't involved in many of the other technologies. The important decisions you make about this technology will affect not only you, but also generations to come.

Donor insemination is intrauterine insemination using semen obtained from a donor. It is one of the most commonly used reproductive technologies but receives very little publicity. Although there are other infertility treatments such as in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) for severe male-factor infertility, donor insemination is often used because it is more affordable.

Anonymous donor insemination is the most common form of donor insemination. Purchase of donor semen and other services are arranged between the sperm bank and yourself. Exact pricing for these things are available from the sperm bank but in general samples cost about $350.00 to $500.00. Additional costs can include shipping and additional donor information.

Known donor insemination is available but is even a more difficult decision process that anonymous donor. It is not necessarily a less costly undertaking as all the Health Canada Guidelines for donor insemination must be followed, At S.O.F.T. we encourage you to think about this very carefully. Counseling is available and may be very useful in this circumstance. You might want to consider legal advice and the development of a legal contract.

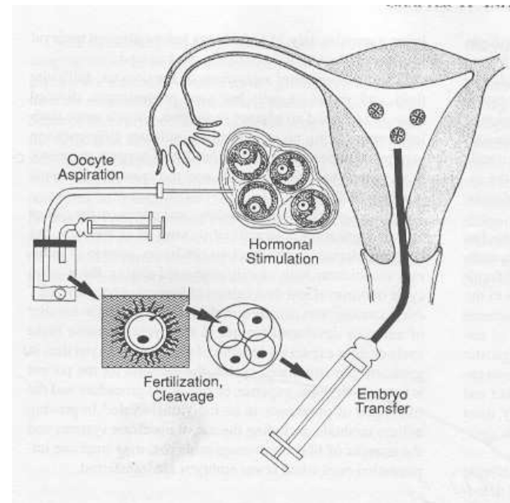
Costs from the S.O.F.T. clinic are only washing the specimen to prepare it for intrauterine insemination ($200.00). Other costs are covered by OHIP.

Success rates with donor insemination range from 10% to 20% per cycle depending on stimulation protocol and whether any female infertility factors are present.

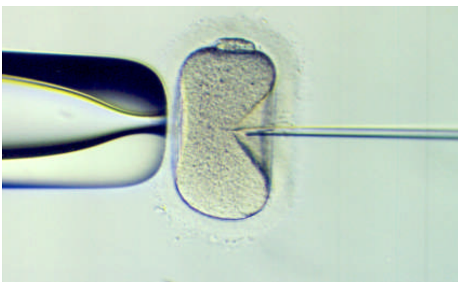
Full information sheets are available from S.O.F.T. about this technology.

3) In Vitro Fertilization with Intracytoplasmic Sperm Injection

In-vitro fertilization (IVF) refers to **the fertilization of the eggs outside of the woman's body**. It is the most complex of the reproductive technologies and is the necessary prerequisite for other newer technologies like intracytoplasmic sperm injection (ICSI). IVF is extremely expensive because it requires expensive medications to stimulate the production of multiple eggs, complex procedures and a state-of-the-art laboratory.



Full information sheets are available from S.O.F.T. about IVF and ICSI.



In IVF, once the eggs have been retrieved they are combined with washed sperm and fertilization takes place. If severe male factor infertility is present, **intracytoplasmic sperm**

injection will be performed. With this technique, a pipette holds the egg and a smaller pipette is used to inject the sperm into the egg. This bypasses the fertilization process and only a single sperm is required for each egg retrieved.

These procedures are usually not covered by OHIP. The IVF cycle costs $4,500.00 and the ICSI procedure costs $1,000.00. (the addition of ICSI to a funded cycle is $1800.00) Additional costs include drugs ($2,800.00 - $4,000.00), travel, accommodation and loss of time from work.

The chance of pregnancy after the sperm are used in an IVF / ICSI cycle is 35-42%. Occasionally, more than three embryos will result from the cycle and these may be frozen and placed in the women's uterus after thawing at some time in the future, improving the overall chance.

Sperm Retrieval

Microsurgical Epididymal Sperm Aspiration (MESA) is a relatively new procedure, which can be performed for infertile couples where the male partner has no sperm in his semen. Males who undergo this procedure must first undergo testing to determine the chance of finding sperm in the epididymis. Investigation should include a hormonal profile, evaluation of testicular size (by physical examination or scrotal ultrasound) and a testicular biopsy. MESA is only appropriate for men with **Azoospermia** (liquid is produced by ejaculation by there are no sperm in the fluid). If there are even a few sperm in the ejaculate or if no fluid is produced when climax occurs, other technologies are more appropriate.

Most men who have no sperm in the ejaculate do make sperm some sperm but just not enough to appear in the ejaculate. The only way to determine if some sperm are being made in the testicle is a testicular biopsy. Decreased sperm production may have many causes, including injuries, exposures, previous surgery, and genetic or developmental problems. If no sperm can be found in the testicle with a testicular biopsy, these men are not candidates for MESA but donor insemination may be considered. If some sperm is found on testicular biopsy, these men should have genetic testing including a karyotype, cystic fibrosis screening and analysis of the Y chromosome. Genetic counseling should also be considered. Buy and large, if a genetic abnormality is found, this is likely going to be passed to any resulting offspring.

However, some azoospermic men produce sperm but there is a blockage between the testicle and the ducts that carry them to the ejaculate. This may be caused by surgery, either accidentally (hernia repairs) or purposely (vasectomy), by congenital absence of the ducts, infection or injury. Men with bilateral congenital absence of the vas deferens are at high risk for being carriers of the cystic fibrosis gene and must be tested for this. These men are candidates for MESA.

The chance of successfully obtaining sperm from this procedure must be individually evaluated. Your physician will provide you with an estimate after your diagnostic work-up is completed. For example, a male with a vasectomy and failed vasectomy reversal has a 90% chance of success but a man with bilateral congenital absence of the vas deferens has about an 80% chance. The chance of finding sperm in a man who is making very few is probably about 60%. Sometimes extra sperm can be

obtained during the MESA or testicular biopsy procedures and they can be frozen for use in future cycles.

There are several options for backup should there be no sperm in the epididymis. Many times, some sperm can be found in the testis and a testicular biopsy can be performed at the time of the MESA procedure to supply these. In men whose chance of finding sperm is very low, donor semen as a backup is sometimes considered.

MESA is not covered by OHIP. The surgical fee for this procedure is set by the specialist you are referred to but generally is about $1,500.00. Additional charges may be incurred from the hospital (operating room charges) and for the anesthetic. Sometimes the MESA can be combined with a scrotal exploration (another surgical procedure) allowing the hospital and anesthetic fees to be covered by OHIP.

The major expense of this technology is incurred because it must be combined with an IVF / ICSI cycle.

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Check out our web site at www.soft-infertility.com