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## A REVIEW ON MALE FERTILITY

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### Abstract

Spermatogenesis is a complex process that involves stem-cell renewal, genome reorganization and genome repackaging, and that culminates in the production of motile gametes. Problems at all stages of spermatogenesis contribute to human infertility. Male infertility, is characterized by hypogonadism, decreased semen quality or ejaculatory dysfunction, accounts for approximately 20% of infertility cases. The main cause for infertility apoptosis. Apoptosis, a form of programmed cell death in contrast to necrosis, which represents "accidental cell death," plays an important role in spermatogenesis. excessive alcohol intake resulted in Leydig cell apoptosis, while cocaine resulted in mitochondrial apoptosis, excessive alcohol intake resulted in Leydig cell apoptosis, while cocaine resulted in mitochondrial apoptosis. Men with severe oligozoospermia less than  $1$  to  $5 \times 10^6$  sperm/ml are considered as a male infertility by diagnosis. Studies on male infertility, potentially opening the door for treatment advances for improving spermatogenesis. Newer techniques like sperm retrieval and VE modifications are promising and becoming increasingly more popular for the estimation of damage of certain DNA is responsible for male infertility.

**Key words:** Male Infertility, Diabetes, Sperm DNA, Impotence.

### 1. Introduction

Infertility primarily refers to the biological inability of a person to contribute to conception. Infertility may also refer to the state of a woman who is unable to carry a pregnancy to full term. There are many biological causes of infertility, some which may be bypassed with medical intervention. Male infertility is a reasonably common problem. Being infertile has nothing to do with male sexual prowess (virility), but rather with the absence of healthy sperm in the semen that are capable of travelling to meet the ovum . Infertility is of four types as follows.

**Infertility** :Reproductive endocrinologists, the doctors specializing in infertility, consider a couple to be infertile if: The couple has not conceived after 6 months of contraceptive-free intercourse if the female is over the age of 35 (declining egg quality of females over the age of 35 account for the age-based discrepancy as when to seek medical intervention).

Alternatively, the NICE guidelines define infertility as failure to conceive after regular unprotected sexual intercourse for 2 years in the absence of known reproductive pathology.

**Sub fertility:**

A couple that has tried unsuccessfully to have a child for a year or more is said to be subfertile meaning less fertile than a typical couple. The couple's fecundability rate is approximately 3-5%. Many of its causes are the same as those of infertility. Such causes could be endometriosis or polycystic ovarian syndrome.

**Primary vs. secondary infertility:**

Couples with primary infertility have never been able to conceive,<sup>[4]</sup> while, on the other hand, secondary infertility is difficulty conceiving after already having conceived (and either carried the pregnancy to term or had a miscarriage). Technically, secondary infertility is not present if there has been a change of partners.

**EPIDEMIOLOGY:**

Approximately 15-20% of couples attempting to achieve pregnancy in the United States each year face difficulties with fertility. Of those couples, a pure "female factor" is responsible for about 35-40% of cases. About another 35% of cases are pure "male factor." Couples with a combination of male and female factors account for the remaining 25-30% of cases. Therefore, a male infertility factor plays a part for more than 50% of couples unable to conceive on their own. These numbers stress the need for appropriate male factor evaluation and treatment options.

**2. CAUSES OF INFERTILITY:**

More than 90% of male infertility cases are due to low sperm counts, poor sperm quality, or both. The remaining cases of male infertility can be caused by a number of factors including they are:

*Environmental pollutants, Exposure to high heat for prolonged periods, Genetic abnormalities Heavy use of alcohol, marijuana, or cocaine, smoking, Hormone deficiency or taking too much of a hormone, Impotence, Infections of the testes or epididymis, Older age, Previous chemotherapy, Previous scarring due to infection, trauma, or surgery, Radiation exposure, Retrograde ejaculation, Smoking, Surgery or trauma, Use of prescription drugs, such as cimetidine, spironolactone, and nitrofurantoin*

**Sperm Abnormalities:**

Sperm abnormalities can be caused by a range of factors, including congenital birth defects, disease, chemical exposure, and lifestyle habits. In many cases, the causes of sperm abnormalities are unknown. Sperm abnormalities are categorized by whether they affect sperm count, sperm movement, or sperm shape they include:

**Low Sperm Count (Oligospermia):** A sperm count of less than 20 million/mL is considered low sperm.

Azoospermia refers to the complete absence of sperm cells in the ejaculate, and accounts for 10 - 15% of cases of male infertility. Partial obstruction anywhere in the long passages through which sperm pass can reduce sperm counts. Sperm count varies widely over time, and temporary low counts are common. Therefore, a single test that reports a low count may not be a representative result.

**Poor Sperm Motility (Asthenospermia):** Sperm motility is the sperm's ability to move. If movement is slow, not in a straight line, or both, the sperm have difficulty invading the cervical mucous or penetrating the hard outer shell of the egg. If 60% or more of sperm have normal motility, the sperm is at least average in quality. If less than 40% of sperm are able to move in a straight line, the condition is considered abnormal. Sperm that move sluggishly may have genetic or other defects that render them incapable of fertilizing the egg. Poor sperm motility may be associated with DNA fragmentation and may increase the risk for passing on genetic diseases.

**Abnormal Sperm Morphology (Teratospermia):** Morphology refers to shape and structure. Abnormally shaped sperm cannot fertilize an egg. About 60% of the sperm should be normal in size and shape for adequate fertility. The perfect sperm structure is an oval head and long tail.

### **Retrograde Ejaculation:**

Retrograde ejaculation occurs when the muscles of the bladder wall do not function properly during orgasm and sperm are forced backward into the bladder instead of forward out of the urethra. Sperm quality is often impaired.

Retrograde ejaculation can be the consequence of several conditions:

Surgery to the lower part of the bladder or prostate (the most common cause of retrograde ejaculation), Diseases such as diabetes and multiple sclerosis, Spinal cord injury or surgery, Medications such as tranquilizers, certain antipsychotics, or blood pressure medications also may cause temporary retrograde ejaculation, Aging.

### **Genetic Disorders:**

Certain inherited disorders can impair fertility. Examples include:

Cystic fibrosis can cause missing or obstructed vas deferens.

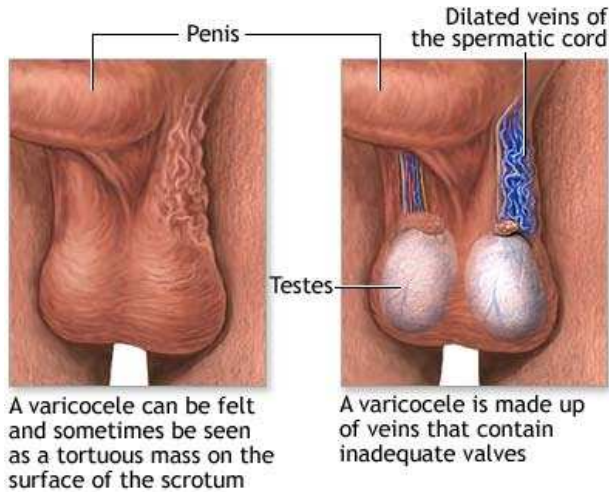
Polycystic kidney disease, a relatively common genetic disorder that causes large cysts to form on the kidneys and other organs during adulthood, may cause infertility as the first symptom if cysts develop in the reproductive tract.

Klinefelter syndrome is marked by two X and one Y chromosomes, which leads to the destruction of the lining of the seminiferous tubules in the testicles during puberty, although most other male physical attributes are unimpaired.

Kartagener syndrome, a rare disorder that is associated with a reversed position of the major organs, also causes impaired sperm motility.

### 3. Risk factors:

#### Varicocele:



A varicocele is an abnormally enlarged and twisted (varicose) vein in the spermatic cord that connects to the testicle. Varicoceles are found in about 15% of all men and in about 40% of infertile men, although it is not clear how much they affect fertility or by what mechanisms. They can raise testicular temperature, which may have effects on sperm production, movement, and shape.

#### Age

Age-related sperm changes in men are not abrupt, but are a gradual process. Aging can adversely affect sperm counts and sperm motility. The genetic quality of sperm declines as a man ages.

#### Sexually Transmitted Diseases

Repeated *Chlamydia trachomatis* or gonorrhea infections are most often associated with male infertility. Such infections can cause scarring and block sperm passage. Human papilloma viruses, the cause of genital warts, may also impair sperm function.

#### Lifestyle Factors

Nearly any major physical or mental stress can temporarily reduce sperm count. Some common conditions that lower sperm count, temporarily in nearly all cases, include:

**Emotional Stress:** Stress may interfere with certain hormones involved with sperm production.

**Testicular Overheating:** Overheating, such as from high fevers, saunas, and hot tubs, may temporarily lower sperm count.

**Substance Abuse:** Cocaine or heavy marijuana use can temporarily reduce the number and quality of sperm. Sperm actually have receptors for certain compounds in marijuana that may impair the sperm's ability to swim and also inhibit their ability to penetrate the egg. Anabolic steroid use can shrink testicles and decrease sperm production. Heavy drinking may also impair fertility.

**Smoking:** Cigarette smoking may affect sperm quality.

Laptops: laptops can also cause male fertility, Men who rest computers on their laps for long periods could be risking their fertility by the increase in temperature 1<sup>0</sup>C may alter the production of the sperm. So the usage of laptops on laps should be avoided by men

### **Environmental Factors:**

Occupational or other long-term exposure to certain types of toxins and chemicals (such as herbicides and pesticides) may reduce sperm count by either affecting testicular function or altering hormone systems. Estrogen-like and hormone-disrupting chemicals such as bisphenol A, phthalates, and organochlorines are particular potential concerns. Chronic exposure to heavy metals such as lead, cadmium, or arsenic may affect sperm quality. At this time, there is no strong evidence supporting a serious harmful effect on fertility in men who have normal limited exposure to these chemicals.

### **Diabetes induced male infertility:**

#### **Sperm+ Sugar= Infertility**

Now a days diabetic mellitus is the most complicatory disease in the world. India one of the leading country suffering with diabetes. More number of complications will arise with diabetic mellitus e.g.: diabetic infertility. Infertility is the most causative disease which effects the reproductive organs of both male and female persons. Diabetes in men has a direct effect on fertility at a molecular level. In diabetes sperm RNA was significantly altered, once altered their ability to repair sperm DNA is collapsed and once this is damaged it cannot be restored.

## **4. DIAGNOSIS OF INFERTILITY IN MALE:**

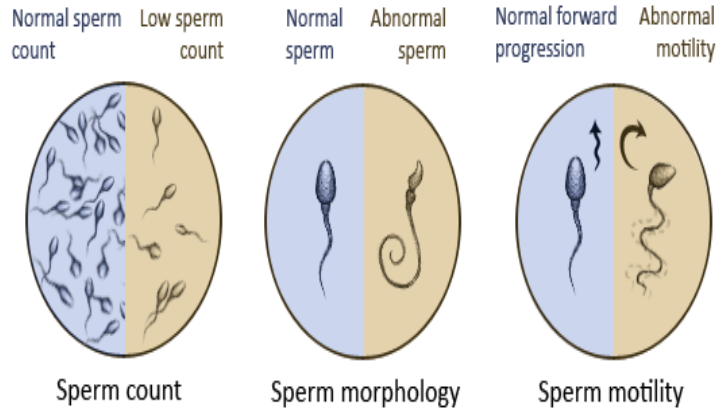
Infertility can be diagnosed by several methods:

### **Semen analysis:**

Although semen analysis is not a test of fertility, a carefully performed semen analysis is a highly predictive indicator of the functional status of the male reproductive hormonal cycle, Most specialists collect at least three specimens in which the seminal parameters are within 20% of each other before establishing a baseline for semen quality. The semen specimen is best obtained by masturbation after a two to three day period of abstinence. Abstinence intervals give large source of variability. With each day of abstinence semen volume increases by 0.4 cc, sperm concentration by 10-15 million per cc, and total sperm count by 50-90 million.

Sperm motility and morphology appear to be unaffected by 5-7 days of abstinence, but longer periods lead to impaired motility. The minimum number of specimens to define good or poor quality of semen is three samples over a 6-8 week interval with a consistent period of abstinence of 2-3 days.

In a longitudinal analysis of semen from both fertile and infertile men, it was found that 97% of men with initial good sperm concentration would continue to show good density after as many as 3-6 specimens.



**Sperm morphology:**

The results of a sperm morphology exam are reported as percent normal. It is always the case that some sperm from an ejaculate are morphologically abnormal, but when that fraction becomes excessive,

fertility may decrease. It is also useful to subclassify the abnormal population into the types of abnormality observed. Two types of classification schemes are commonly used: Abnormalities can be classified as affecting the head, midpiece or tail. The most basic type of classification scheme differentiates primary and secondary abnormalities:

Anatomic site of the defect: The problem can involve the **head, midpiece or tail**. Some abnormal sperm may have defects in more than one site.

Primary versus secondary defects: Primary defects are the more severe and are thought to originate while the sperm was still within the semeniferous epithelium of the testis. Secondary defects are less serious and thought to arise during passage through the epididymis or by mishandling after ejaculation.

**Sperm Morphology**



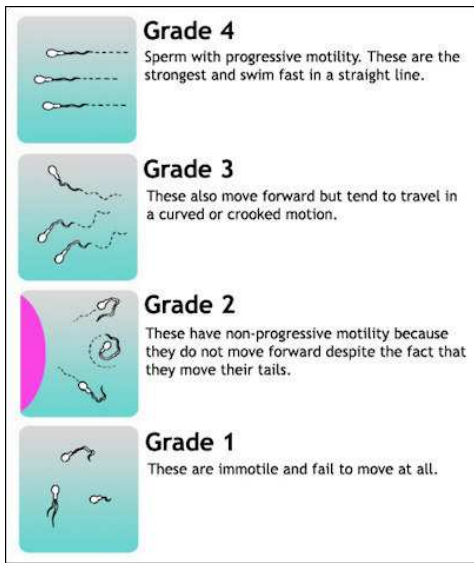
**Sperm motility:**

It is usually rated in two ways: the number of motile sperm as a percentage of the total, and the quality of forward progressive sperm movement i.e., how fast and how straight the sperm swims.

The degree of forward progression is a classification based on the pattern displayed by the majority of motile sperm. It ranges from zero (no movement) to 4 (excellent forward progression). Typically, we have to observe at least 50% of the sperm with good forward progression.

Microscopic evaluation of the liquefied semen may reveal agglutination of sperm. Agglutination may be head-to-head, head-to-tail, or tail-to-tail and may suggest an inflammatory or immunologic process. Sperm morphology is subject to great variation and it is unusual to see specimens that contain more than 80% normal sperm heads.

**Sperm count:**



Sperm count or sperm concentration to avoid mixup, measures the concentration of sperm in a man's ejaculate, distinguished from *total sperm count*, which is the sperm count multiplied with volume. Over 15 million sperm per milliliter is considered normal, according to the WHO in 2010. A lower sperm count is considered oligozoospermia. A vasectomy is considered successful if the sample is azoospermic. Some define success when rare non-motile sperm are observed (fewer than 100,000 per millilitre). Others advocate obtaining a second semen analysis to verify the counts are not increasing and others still may perform a repeat vasectomy for this situation.

The average sperm count today is around 60 million per millilitre in the Western world, having decreased by 1-2% per year from substantially higher number decades ago.

Chips for home use are emerging that can give an accurate estimation of sperm count after three samples taken on different days. Such a chip may measure the concentration of sperm in a semen sample against a control liquid filled with polystyrene beads.

**5. Treatment:**

Infertility can be treated by various methods as it is a common disorder found across the world. There are some of the therapies listed here.

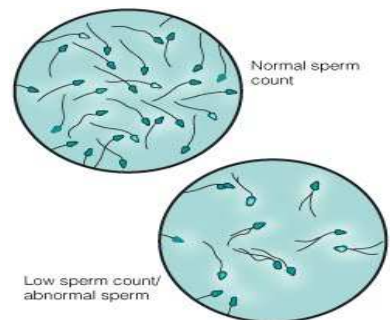
**Non-surgical/ Medication Therapy:**

**Spinal Cord Injury (SCI) Treatments:**

Many factors may predispose spinal cord injured men to infertility.

Ejaculatory dysfunction, abnormalities of sperm production, chronic infections and blockage of sperm within the male reproductive tract are all potential factors.

There is a number of different methods to obtain sperm, often combined with various forms of assisted reproductive techniques.



For example, sperm can often be obtained through vibratory stimulation to the head and shaft of the penis if the level of injury is T-12 or above. Other therapies commonly used it the rectal probe. Electro ejaculation (EEJ) or sperm harvesting along the ejaculatory path from the vas deferens, epididymis, and directly from the testis.

### **Electro ejaculation therapy (EEJ):**

This is a very successful form of therapy for men who have normal sperm production but cannot ejaculate because of a short circuit in the nervous system. Initially used for men with spinal cord injuries, EEJ has also proven effective for loss of ejaculation in patients with other conditions such as diabetes, retroperitoneal lymph node dissection (RPLND), pelvic surgery, multiple sclerosis, or unexplained loss of orgasm. For patients with intact sensation, a pain free procedure of 30 minutes with local anesthesia at an outpatient surgery centre. EEJ is non-invasive and patients routinely return back to desk type work that day.

Electroejaculation allows the retrieval of sperm in more than 90% of patients and up to 40% of couples will achieve pregnancy with IUI. The very powerful sperm injection form of IVF, called ICSI, gives the remaining couples a 50% chance for pregnancy. Overall, the chances for pregnancy in the informed and motivated patient are similar to those of a healthy male.

### **Transurethral Resection of Ejaculatory Duct:**

#### **Transurethral resection of the seminal vesicles (TURS):**

The procedure eliminates obstruction in the seminal tract or in a strategic area, improving the chances of the inflamed or chronically dilated zones to normalize.

### **Medication:**

#### **Hormone deficiency treatments:**

If the man has a hormonal deficiency, it might be treatable with medications. These are rare cases.

### **Clomiphene citrate (Clomid, Serophene):**

Some men with relatively mild sperm abnormalities have been treated with clomiphene citrate(tablets) in an attempt to improve the semen. Research showed that Clomid for the male sometimes can improve the sperm count or motility.

### **Surgery:**

#### **Varicocele ligation:**

If a varicocele is found, sometimes surgery to ligate (tie off) the abnormally dilated veins is recommended. If the varicocele is of significant size (Grade II or Grade III), about two thirds of men undergoing the surgery will see improvement in the sperm quality. Pregnancy rates following surgery are in the range of 40%, but most pregnancies occur 6-9 months following surgery depending on the female's age.



If the initial sperm count and motility are in the severe male factor category, it is unlikely that this surgery will improve sperm counts enough to enable the couple to conceive without assistance.

### **Sperm Retrieval Techniques (MESA, PESA, TESE):**

Using today's minimally invasive techniques, sperm can be obtained from men with vasectomy; failed vasectomy reversal, absence of the vas deferens, or uncorrectable blockages anywhere along the seminal tract (obstructive azoospermia). In addition, we are able to retrieve and use sperm in case of non-obstructive Azoospermia or NOA.

Sperm retrieval procedures are typically done at an outpatient surgery and last about one hour. Local anesthetic, IV sedation or general anesthesia provides complete pain control during the procedure. Patients return back to desk type work in a day or two.

### **Prevention of male infertility:**

Most types of infertility cannot be prevented. Smoking has been linked to low sperm counts and sluggish sperm movement in men, and an increase in miscarriage in women. , Alcohol affects the fertility of both men and women trying to conceive either naturally or through infertility treatments. Alcohol is toxic to sperm; it reduces sperm counts, can interfere with sexual performance, Other useful methods include meditation, relaxation, moderate physical activity and yoga, A well-balanced diet includes carbohydrates, protein and fibre., Avoid environmental poisons and hazards such as pesticides, lead, heavy metals, toxic chemicals, and ionising radiation

### **References:**

1. Makar RS, Toth TL (2002). "The evaluation of infertility". *Am J Clin Pathol.* 117 Suppl: S95–103.
2. Cooper TG, Noonan E, von Eckardstein S, et al. (2010). "World Health Organization reference values for human semen characteristics". *Hum. Reprod. Update* 16 (3): 231–45.doi:10.1093
3. *Fertility: Assessment and Treatment for People with Fertility Problems.* London: RCOG.
4. Bendsdorp AJ, Cohlen BJ, Heineman MJ, Vandekerckhove P. Intra-uterine insemination for male subfertility. *Cochrane Database Syst Rev.* 2007 Oct 17.
5. Jain T, Gupta RS. Trends in the use of intracytoplasmic sperm injection in the United States. *N Engl J Med.* 2007 Jul 19;357(3):251-7
6. Khera M, Lipshultz LI. Evolving approach to the varicocele. *Urol Clin North Am.* 2008 May;35(2):183-9, viii.
7. Levine BA, Grifo JA. Intrauterine insemination and male subfertility. *Urol Clin North Am.* 2008 May;35(2):271-6.
8. Schiff JD, Ramirez ML, Bar-Chama N. Medical and surgical management male infertility. *Endocrinol Metab Clin North Am.* 2007 Jun;36(2):313-31.
9. Van Peperstraten A, Proctor ML, Johnson NP, Philipson G. Techniques for surgical retrieval of sperm prior to intra-cytoplasmic sperm injection (ICSI) for azoospermia. *Cochrane Database Syst Rev.* 2008 Apr 16;(2):CD002807.
10. Zhu JL, Basso O, Obel C, Bille C, Olsen J. Infertility, infertility treatment, and congenital malformations: Danish national birth cohort. *BMJ.* 2006 Sep 30;333(7570):679. Epub 2006 Aug 7
11. <http://www.ivf.com/shaban.html>.
12. Nathan Birch, JD Niemand Aug 29, 2010 [www.cracked.com/article18701](http://www.cracked.com/article18701).
13. <http://www.cincinnatiinfertility.com/causes-of-infertility/male-infertility>.
14. Martinbastuba, Male Fertility & Sexual Medicine Specialists, <http://www.malefertility.md/treatment-options-male-infertility.html>.
15. [health-cares.net/infertility-prevention.php](http://health-cares.net/infertility-prevention.php), Jul 18, 2005