Varicocele and Male Factor Infertility

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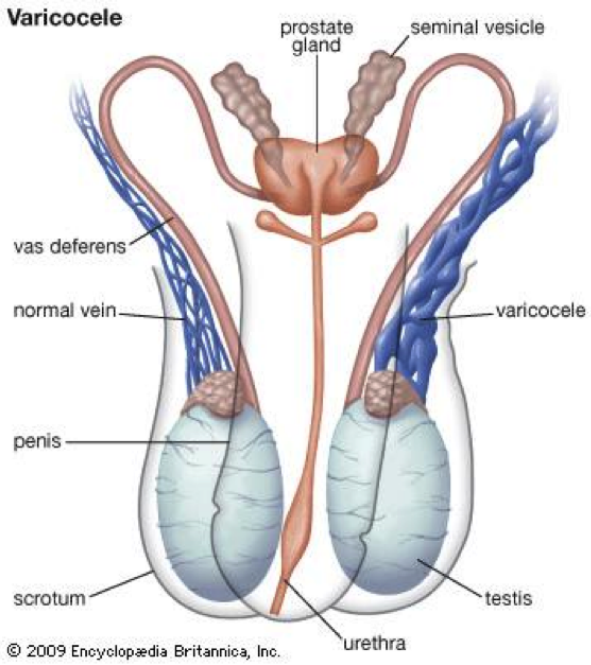
Varicocele and male factor infertility: Many men (40%) with low sperm count, low movement and high abnormal sperm shape have dilated veins around the testes. On the other hand, many men (15%) with varicoceles have normal sperm parameters and fertility. Only large varicoceles than can be felt by a physician are associated with lower fertility in men. Varicoceles are found during physical examination and can be confirmed with Doppler ultrasound of the testes. How dilated veins – varicoceles may cause abnormal sperm and male infertility is still unknown for sure (pressure, heat, toxin accumulation, oxidative stress).



varicocele surgery

Does surgical treatment of varicocele increase the chance of pregnancy in female partners?

Some urologists recommends surgical treatment of varicoceles in adult men to improve the chance for spontaneous conception

This recommendation should at least be issued if and only if:

1. Varicocele was large enough to be felt on examination (not ultrasound).
2. The couple had documented infertility or desire future fertility.
3. The female partner had normal fertility (especially normal egg reserve) or correctable infertility.
4. The male partner had one or more abnormal semen parameters.

The rationale is that repair may restore normal sperm parameters and spontaneous conception. *Varicocele repair is definitely not indicated in the presence of female factor requiring IVF* e.g blocked fallopian tubes, as improved sperm parameters will not achieve a pregnancy. Some studies reported improved sperm parameters and sometimes fertility after surgical treatment of varicocele but many of them were low quality studies (no control group, not randomized, non-palpable varicocleles).

Good quality studies: randomized (one group of men underwent surgery for large varicoceles and another group did not)

Ten randomized studies were published (including 894 men). Some studies indicated improve in sperm parameters after surgery. Most of the studies indicated that the chance for live birth is not increased after varicocele repair. There is no conclusive evidence that varicocele repair increases the chance for pregnancy and delivery in female partners of men

diagnosed with varicoclele (summary below).

Surgery or embolization for varicoceles in subfertile men: Varicocele is a dilatation (enlargement) of the veins along the spermatic cord (the cord suspending the testis) in the scrotum. Dilatation occurs when valves within the veins along the spermatic cord fail and allow retrograde blood flow, causing a backup of blood. The mechanisms by which varicocele might affect fertility have not yet been explained, and neither have the mechanisms by which surgical treatment of the varicocele might restore fertility. This review analysed 10 studies (894 participants) and found evidence (combined odds ratio was 1.47 (95% CI 1.05 to 2.05) to suggest an increase in pregnancy rates after varicocele treatment compared to no treatment in subfertile couples, in whom, apart from poor sperm quality, varicocele in the man was the only abnormal finding. This means that 17 men would need to be treated to achieve one additional pregnancy. However, findings were inconclusive as the quality of the available evidence was very low and more research is needed with live birth or pregnancy rate as the primary outcome (Kroese 2012).

Surgical repair of varicocele should only be considered in carefully selected subfertile couples. There is no conclusive evidence that repair increases the chance for delivery in female partners. Data supporting surgical repair of varicocele are controversial and results or surgery is certainly inferior to IVF-ICSI.

A consultation with reproductive endocrinologist & fertility specialist is very important before deciding on varicocele surgery to study female factor infertility and discuss potential benefits and harm from surgery in achieving the final goal which is conceiving not just improving sperm count and motility.

varicocele and Male Factor Infertility

Male Factor Infertility: Azospermia

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Male Factor Infertility: Azospermia means no sperm are found in the ejaculate. Azospermia requires careful evaluation and treatment so that the couple has the best chance to conceive with IVF. The evaluation should be methodical and compassionate to guide the couple through such a multifaceted process to pregnancy and delivery of a healthy child.

Four Things Have to Happen at Initial Evaluation for Azospermia

a. Is it truly azospermia? sometimes repeat sperm analysis together with spinning of the ejaculate multiple times may yield few sperm. This has to be performed by a diligent andrologist and in a facility that can freeze sperm immediately if found. In some azospermic men, repeat analysis and freezing can avoid a surgical procedure to retrieve sperm.

b. A genetic cause for azospermia should be excluded. Specifically three known genetic problems should be excluded because they can be passed to offspring and because they can predict the success of surgical sperm retrieval. A chromosome analysis should be done to exclude sex chromosome abnormalities e.g klinefelter Syndrome (47XXY). Y chromosome microdeletion study should be conducted to exclude a deletion of the part of Y chromosome related to sperm production. Cystic fibrosis carrier screening should also be run to detect defect in the CF gene that may be associated with absence of

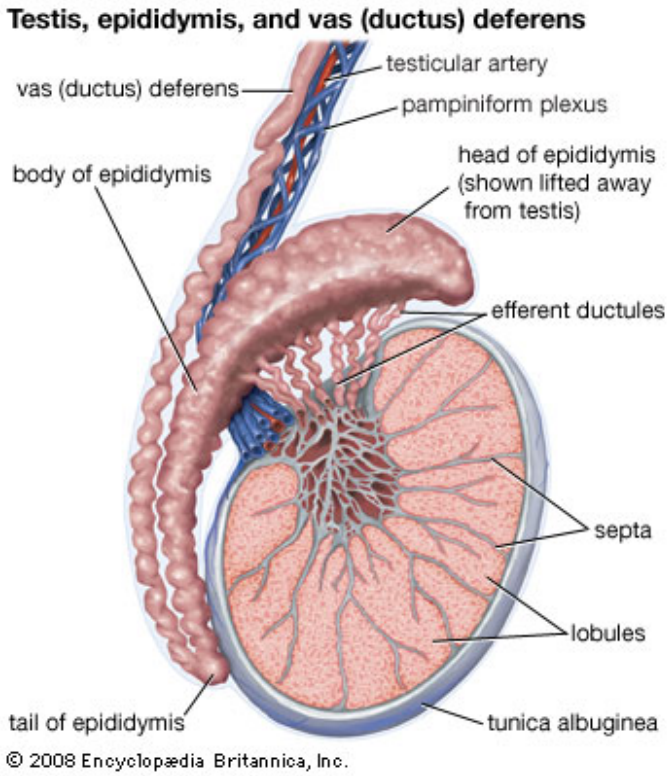
the ducts conducting the sperm outside of the testes.

c. Evaluation of Ovarian Reserve for Female Partner. If ovarian reserve evident by day 3 FSH, AMH levels and antral follicle count seen on vaginal ultrasound is not diminished, this predicts reasonable chance for success with IVF-ICSI if sperm are found. Extremely low ovarian reserve or advanced female age may preclude surgical sperm retrieval, unless an donor eggs are acceptable.

d. Urological evaluation. This has to be the last step in evaluation. Male urologists are the physicians specializing in evaluating the chance for successful sperm retrieval (TESE) as well perform these procedures. Before referral by a reproductive endocrinologist and infertility specialist, there should be every reason to think that if sperm were obtained there is a reasonable chance for conception after IVF-ICSI. The urologist should be a specialist in male reproduction and well versed in the techniques of sperm retrieval. You actually need to ask your urologist two questions: what are my personalized chance for finding sperm when surgery (TESE) is performed? What the technique used to obtain sperm? Authorities generally agree that the technique for TESE markedly affect the chance for finding sperm.

Moreover, every workup should end with an important question; would you accept donor sperm if no sperm were obtained after surgery?

How is TESE Performed?



Testes and ducts

Testicular sperm extraction is a surgical procedure that entails sampling of multiple areas of the testes aiming at finding sperm to be used for IVF-ICSI. The tested is delivered outside the scrotum, bisected and multiple biopsies obtained from several areas of the testes. The tissue is examined for the presence of sperm. If no sperm were found, more biopsies are obtained till sperm are found. There are generally two types of azospermia: obstructive azospermia (due to obstruction of the ducts of the testes while sperm production is intact). Sperm is obtained in close to 100% of these cases. Non-obstructive azospermia (NOA) where is a defect in sperm production, approximately 60 to 70% of the procedures yield sperm.

Blind biopsy from one area of the testes has no place in modern treatment of azospermia. Asking your urologist about the technique of TESE is of paramount importance. The first surgical attempt carries the highest chance for success.

Recently, Doppler ultrasound mapping of the testes can help localize the areas of that should be biopsies because they

yield a higher chance for finding sperm.

Why is IVF-ICSI Required after Sperm Retrieval?

The number of sperm obtained after TESE is small in the magnitude of tens to hundreds of sperm, too small to use the sperm for IUI. ICSI is absolutely required for all cases of surgical retrieval of sperm. The sperm can be used in one of two ways

a. Frozen TESE sperm: The sperm are frozen to be thawed at a later date, on the day of egg retrieval for the female partner. This method saves the cost of IVF if no sperm were retrieved and donor sperm use is unacceptable.

b. Fresh TESE sperm: Ovarian stimulation is started and TESE is performed on the day of egg retrieval or the day before. Fresh sperm are used for ICSI. Donor sperm (if acceptable) is obtained as a backup. Though suggested, there no concrete evidence that fresh TESE sperm is superior to frozen TESE sperm.

In addition in some caes with associated genetic problems, preimplantation genetic diagnosis (PGD) can be performed followed by the transfer of normal embryos.

Can the Chance for Pregnancy be predicted in Male Factor Infertility: Azospermia ?

There are several predictive factors for pregnancy in female partners of men with azospermia. These can be categorized into:

i. Successful sperm retrieval is related to whether the procedure is the first one or a repeat procedure, the volume of the testes, medical treatment before surgery, the technique used and the cause for azospermia. Some causes are associated

to minimal chance for obtaining sperm.

ii. Pregnancy after sperm retrieval is related to the female partner age and her ovarian reserve. Younger women have a very good chance of conceiving if sperm are obtained. This is the most important factor once sperm are retrieved.

iii. Obstructive azospermia has a higher chance for sperm retrieval than non-obstructive azospermia.

iv. Moving sperm at the time of ICSI has a higher chance to yield a pregnancy than non moving sperm

v. Men with higher testosterone levels and lower LH levels has higher chance of sperm retrieval

vi. The effect of using of frozen TESE sperm is controversial. Some authorities think that using a fresh TESE sperm is better than frozen sperm.

vii. Use of Doppler: recent work indicates that the use of Doppler study of the testes before the procedure may help localize the areas that should be biopsies and yield a higher chance for sperm harvest.

> *Male Factor Infertility: Azospermia requires a multidisciplinary approach; first consultation with a reproductive endocrinologist (female age is still the most important factor) followed by a consultation with a reproductive urologist for the TESE procedure for successful sperm harvest and pregnancy*

Testosterone Therapy-Male Infertility

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Many men are prescribed testosterone for a variety of reasons. Low testosterone levels (Low T) with no symptoms, general symptoms of low energy and feeling tiered and sexual symptoms, among others. Approximately 2.5 million men are prescribed testosterone each year in The US, mostly with no proper testing. Testosterone is only approved by FDA for low testosterone associated with specific diseases affecting testicular function. The FDA recently issued a safety communication cautioning the use of testosterone replacement for low testosterone levels and requiring labeling change to inform men of a possible increase in side effects.

From the fertility standpoint, there is no role for testosterone treatment, that could be detrimental. There is also no *proven* role for other medical treatment as clomid, letrozole, nolvadex, hCG and others in enhancing fertility in the vast majority of men

Effects of testosterone on male fertility

When men are prescribed testosterone, sperm production slows down significantly and may completely stop. Many of them, no sperm can be found in the ejaculate (azospermia). Testosterone therapy can markedly lower the ability of men to father children. Testosterone inhibits a key master gland hormone (FSH) that is required to stimulate spermatogenesis (making sperm). The specific effects of testosterone on sperm count are unpredictable. In some men sperm count drops to zero even after a short use of testosterone.

Interestingly, when testosterone is stopped some men but

definitely not all of them recover sperm production, commonly in one to six months. The extent of the recovery of sperm count is also unpredictable. The recovery of sperm count maybe limited requiring fertility treatment for conception to take place. A short course of testosterone can lead to a low sperm count for a very long time.

What can be done about low sperm count related to testosterone treatment

In addition to evaluation of female factors especially ovarian reserve, always a priority, men on testosterone and showing low sperm count should be advised to

1. Stop testosterone administration immediately

2. Repeat sperm analysis in 2 months. Sperm analysis should be performed in a facility that can perform diligent search for even very few sperm and can freeze sperm. If sperm is found in the ejaculate it should be cryopreserved immediately. If no sperm is found then sperm analysis should be repeated in another 2 months. The wait for recovery cannot be indefinite because of further deterioration of ovarian reserve in female partner with time.

3. Depending on the extent of recovery sperm can be utilized to promote conception. If sperm count recover close to 10 million moving sperm, natural conception can take place. Also sperm can be used for IUI, if needed. If the number of motile sperm is significantly lower, IVF is required, sometimes with intracytoplasmic sperm injection (ICSI).

4. If still no sperm were found after repeat analysis, TESE (testicular sperm extraction) can be attempted. A male reproductive urologist can perform diligent search for areas of spermatogenesis in the testes through repeat minute biopsy and searching under the microscope.

From the preventive aspect, avoid testosterone treatment if

you intend to father children in the future. Know that there are very few solid indications for testosterone. If testosterone treatment is inevitable, consider pretreatment sperm freezing. Use gel preparation preferential to injection as they are not stored for a long time in the body.

Testosterone treatment is a preventable cause for infertility in males and could be detrimental to future fertility.

Practical Approach to Male Infertility

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Male factor infertility is present in approximately 40% of couples having difficulty to conceive. In most cases, however, it is seldom one factor. A basic element that is encountered in every case is the number and quality of eggs. Other factors in also include sexual factor and other female factors (e.g blocked fallopian tubes). Hence, evaluation of female factors is integral to evaluation and successful treatment of male factor.

Evaluation of female factors includes testing for ovarian reserve and testing of the fallopian tubes for patency. In addition to evaluation of medical, obstetric and genetic risks of getting pregnant.

Evaluation of Male Factor

Reproductive ability in males is initially evaluated through i. Detailed history of male partner and ii. sperm analysis. History can indicate many factors that may reduce the ability to conceive: social habits, erectile dysfunction, childhood infections (mumps), medical disorders, genetic diseases (chromosomal abnormalities, specific genetic diseases as cystic fibrosis), occupational exposure..etc. Unfortunately in the majority of cases history may not predict abnormalities in male factor

Sperm Analysis

Accurate interpretation of sperm analysis (volume, concentration, movement and shape) is the most important step in evaluation. It is important to take in consideration each factor separately and then in combination. Normal parameters are volume >2mL, concentration 15million/mL, motility 40% and normal shape 4% using strict morphological criteria (Kruger).

Repeat sperm analysis is commonly recommended when abnormalities are detected. There is no strong evidence to repeating the sperm analysis. If the sperm analysis is to be repeated this should be done at least 2 months later as it would take that long for new sperm to be 'manufactured'.

Generally 10 million moving sperm sperm per ejaculate (volume x concentration x % motility) is required for successful reproduction with intercourse and IUI. Approximately 2 million motile sperm are adequate for IVF. Lower parameters especially if low morphology <2% require IVF with intracytoplasmic sperm morphology (ICSI).

Other Tests

Genetic screening for chromosome analysis and Y chromosome micro-deletion is required in low sperm concentration (<10 million /mL) and azospermia is required. Abnormalities are

found in 5-10% of men and can be transmitted to children. Genetic screening for cystic fibrosis and its congenital absence of the vas deferens is also required if azosprmia (obstructive) is present.

Other sperm tests as pH, fructose and sometimes hormone analysis are sometimes helpful.

Tests for sperm DNA fragmentation is still being evaluated but are not part of routine fertility workup.

Treatment of Male factor Infertility

Improvement in sperm analysis is not the main aim of treatment. The main aim is conception and delivery of a healthy child. Sperm analysis improvement is a surrogate outcome not a final goal. In most cases, the improvement in sperm parameters (count, movement and shape) does not translate into a higher chance for conception. In addition, in the majority of cases there is no specific cause identified for male factor abnormalities. The two practical strategies left are to wait (within what is allowed by female ovarian reserve) for sperm analysis to improve and conception to occur or to use the small / abnormal sperm available for assisted reproduction (ICSI) which is a very efficient strategy.

Four Important Considerations before Treating Male Infertility

a. Female age and ovarian reserve: any treatment for male factor should be guided with the number of eggs in the ovary and their quality (age related). In women with women with low egg reserve and 35 or older consideration to ovarian stimulation (to increase mature egg production) followed by IUI or ICSI should be exercised.

b. Sperm Freezing: In men with moderate to severe male factor one should consider freezing one or more sperm samples. The future sperm parameters cannot be predicted and can deteriorate even to a complete absence of sperm in ejaculates.

Sperm freezing is cheep, non invasive and can save men from the need for surgical retrieval of sperm. Men undergoing vasectomy can also consider sperm freezing, prior to procedure, in case they decide to father children in the future

c. Genetic screening: there are two main values to screening males with moderate to severe sperm abnormalities to chromosomes, Y micro-deletion and cystic fibrosis. To avoid transmission to children and to counsel the couple about the chance of successful surgical sperm retrieval (TESE). In some cases the chance for finding sperm is extremely low that TESE is not indicated.

b. Urological consultation: After female and initial male evaluation is complete, evaluation by a male urologist is very useful. A urologist well versed in male infertility can counsel the couple about the chance for success of surgical sperm retrieval and following correct of obstruction.

Four Treatment Options to Consider

Surgical sperm retrieval: in obstructive and non-obstructive azospermia sperm can be retrieved directly from the testes by a male urologist. Micro-TESE involves dissecting one or both testes and obtaining multiple tiny biopsies from many areas. In real time each biopsy is examined under a microscope. The process is repeated till sperm are obtained. The best chance

Surgical treatment for obstructive azospermia: in men that underwent vasectomy before vasectomy reversal can, if successful, restore fertility. Other areas of obstruction can also be restored by urological surgery.

IUI: in few cases of mild male infertility (producing close to 10 million motile sperm) or mild shape abnormalities, ovarian stimulation and IUI is an aoption for 3 cycles. IUI using donor sperm is also an option.

IVF-ICSI: assisted reproductive technology is very robust and can address the majority of male infertility: low sperm count, low motility, abnormal sperm shape, prior fertilization failure. Its is very efficient that it can achieve a conception with very few available fresh or frozen sperm. It can be synchronized with surgical sperm retrieval so that fresh sperm are used for ICSI. Once sperm are available, the success of IVF is dependent on female age and ovarian reserve.

Interventions to Avoid or Consider Cautiously

Surgical treatment of varicocele: Varicocele is a common finding in infertile males and can be associated with low concentration and motility and higher abnormal shape of sperm. Varicocele surgery does improve sperm parameters. The problem with varicocele surgery is that it is not proven to increase the odds of delivering a child by female partner. Varicocele surgery should be cautiously considered due to lack of solid evidence of its benefits.

Medical treatment: The use of medications (e.g clomid, nolvadex, anastrozole) should be avoided as there is no evidence that they will improve the chance of pregnancy and improvement in sperm parameters. The use of injection medications should only be employed in men with a specific indications related to deficiency of such hormones

Supplements: so far there is NO supplement or ‘vitamin’ proven to increase the chance for successful reproduction in male with sperm abnormalities.

A practical approach to male infertility requires initial evaluation of sperm analysis, ovarian reserve and genetic risk factors followed by a treatment plan oriented with the ultimate goal: conceiving healthy child not intermediate issues as cause of male infertility and improving sperm analysis.

How to Preserve Fertility After Prostate Cancer

How to Preserve Fertility After Prostate Cancer Diagnosis

Prostate cancer is the most common cancer in men, 1 in 6 men in the US. Treatment of **prostate cancer** can markedly reduce fertility potential. Its is expected that 217,000 men were diagnosed with prostate cancer in the US in 2010.
Screening for prostate cancer using a blood tests-prostate specific antigen (PSA) resulted in increased diagnosis in younger men. **Many men diagnosed with prostate cancer are interested in future fertility**. Prostate cancer is diagnosed in 1 in 10,000 men before the age of 39 and 1 in 40 between the ages of 40 and 59. Except in cases of distant spread, survival after prostate cancer approaches 100%. Prostate cancer is more common in men carrying BRCA2 mutations and occurs in younger age.
Cancer in men may affect sperm count and quality, although this is controversial. In general 10% of men diagnosed with cancer are expected to have no ejaculated sperm-azospermia. Up to 50% may have abnormal sperm quality.

Effects of prostate cancer treatment on future fertility in men

Treatment options for prostate cancer include

1. *Radical prostatectomy*. This procedure can be performed through a large incision or via minimally access surgery. Surgery can be modified to preserve the nerve

fibers responsible for erection thus reducing erectile dysfunction after surgery. Surgery causes block of the vas deferens and ejaculatory ducts; the ducts that convey sperm out of the testes, leading to obstruction and azospermia.

2. Radiation. *External beam radiation* affect sperm production from the testes as scattered radiation can damage the sperm producing cells. Placing a *radioactive seed inside the prostate – brachytherapy*, has minimal effect on sperm production.
3. Observation only is possible for selected men diagnosed with prostate cancer.

Options for fertility preservation in prostate cancer

1. *Sperm Cyopreservation*. Less than 50% of men diagnosed with cancer preserve their sperm before treatment due to lack of information or counseling. This is a very available and low cost option. One or more samples can be frozen depending on time and initial sperm counts and quality. Sperm can be frozen indefinitely. If multiple samples were frozen, they can be used for intrauterine insemination. If limited amount of sperm is available or low quality -movement or sperm shape, IVF with injection of sperm into the egg-ICSI is required. **Sperm freezing has a good psychological impact on men during cancer treatment**.
2. *Electroejaculation*. For men who have erectile dysfunction or inability to ejaculate after surgery, electrical stimulation can induce ejaculation. Sperm quality in this case is likely abnormal favoring the use of sperm for IVF-ICSI.
3. *Testicular Sperm Extraction-TESE*. Form men with no ejaculated sperm – azospermia, sperm can be surgically obtained from the testes. This is also an option for men who cannot produce sperm and no sperm could be aspirated

without surgery. This procedure can be performed during the surgical treatment for cancer. Sperm are obtained in 60% of men with azospermia. Sperm obtained are used for IVF with ICSI. Sperm can also be obtained from the duct that convey sperm outside the testes-*Microsurgical epididymal sperm aspiration-MESA*. The success rate of achieving pregnancy using frozen ejaculated sperm or surgically obtained viable sperm is not different from fresh sperm. This is also an option for reproduction in men who did not freeze sperm before surgery.

Checklist for fertility preservation in prostate cancer

- Discuss with your oncologist different cancer treatment options-radical prostatectomy, external beam radiation and brachytherapy or even observation only.
- If radical prostatectomy is planned inquire about the technique of surgery-open or laparoscopy, nerve sparing procedures and incidence of erectile dysfunction in the surgeon’s hands
- Ask for more information about the effects of prostate cancer treatment and fertility preservation options from the oncologist or reproductive endocrinologist.
- If interested in fertility preservation a reproductive endocrinologist or urologist can refer you for semen analysis and freezing (in the same time), interpret the semen analysis and advice about the number of samples to be frozen.
- If no sperm found-azospermia, surgical sperm retrieval can be performed at the time of surgery for cancer.

Sperm Analysis in Natural and Assisted Conception

Sperm analysis is the initial test for evaluation of male fertility. Components of **sperm analysis** include volume, count (concentration), movement and shape of sperm cells.

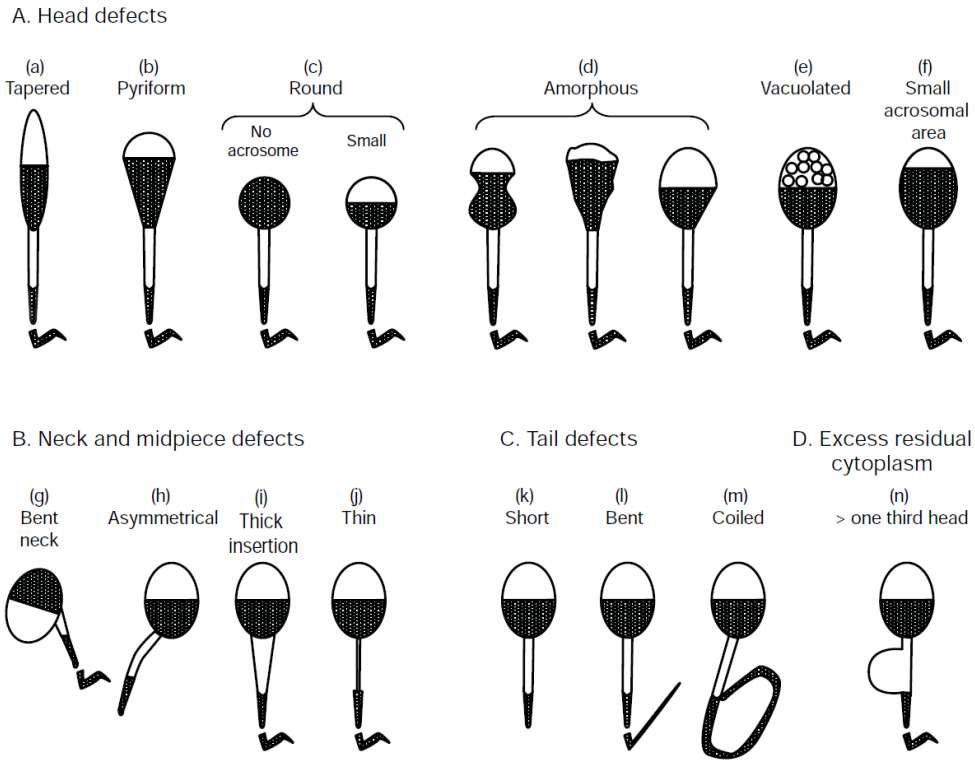
Normal Sperm Analysis

Sperm volume: the total amount of fluid produced. Commonly 1.5 mL or more.

Sperm count: number of sperm in each mL of fluid. Normal concentration is 15 to 20million per mL. Total count= volume x concentration (count).

Sperm motility: % of sperm with vigorous or moderate movement. Total motile sperm count=volume x concentration x %motility

Sperm morphology: Shape of sperm using strict (Tygerberg, Kruger) criteria 4% normal or more



Strict Sperm Morphology

Lower reference limits for men whose partner conceived within 12 months after stopping use of contraception had the following parameters (WHO manual , 5th ed.) are:
Semen volume (ml) 1.5 (1.4–1.7)

Total sperm number (10^6 per ejaculate) 39 (33–46)

Sperm concentration (10^6 per ml) 15 (12–16)
Total motility (PR + NP, %) 40 (38–42)
Progressive motility (PR, %) 32 (31–34)
Vitality (live spermatozoa, %) 58 (55–63)
Sperm morphology (normal forms, %) 4 (3.0–4.0)

All parameters should be interpreted in conjunction with clinical information. If abnormal it can be repeated in 2 to 3 months.

How much sperm is enough?

Evaluation of male fertility through sperm analysis is complex. Clinical factors in history and examination should be considered. Total sperm count in the specimen is an important

factor e.g low sperm morphology in specimen of 200 million sperm may have a different effect than low morphology in a specimen of 30 million sperm. Although there are notable variations in a sperm sample of the same man over time, there is no evidence that repeat evaluation of semen in helpful in managing infertility in a female partner.

Since we have very limited tools (medications, supplements, surgery) to meaningfully improve sperm parameters and fertility, a practical management of fertility due to male factor is:

>10 million motile sperm: suitable for natural conception and IUI

2-10 million motile sperm: suitable for IVF

<2million motile sperm or strict morphology <2% suitable for IVF with ICSI (intracytoplasmic sperm injection)

IVF + ICSI is indicated if surgical sperm harvest is needed and some cases or retrograde ejaculation and anti-sperm antibodies.

Can the sperm analysis be improved?

The count, motility and morphology can sometimes be improved (lifestyle modifications, medicine, surgery). Two important tips to consider though

a. In the majority of cases, there is no evidence that this improvement increases the odds of a pregnancy in female partner

b. The delay in treatment is sometimes critical for women with low egg reserve while they wait for their partners to improve there sperm parameters

Fertility in Men Diagnosed with Cancer

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Who needs to consider preservation of Fertility?

a. The American Cancer Society estimates that 760,000 men will be diagnosed with cancer in 2009. Cancer itself (before treatment) is sometimes associated with less sperm production in men. This is specially the case in Hodgkin's lymphoma, testicular cancer, prostate cancer, leukemias and colon cancer. The most harmful factor, however, is cancer treatment. Chemotherapy and radiation significantly impair sperm production. The effect of chemotherapy depends on age, drug used, dose and duration. Cyclophosphamide appears to be the most harmful agent. Radiation also impairs sperm production especially at doses of 1200cGy or more.

Sperm count sometimes recover to a variable extent years after cancer treatment. This depends on the type of cancer and treatment used. For example 90% of men diagnosed with Hodgkin's lymphoma, treated with MOPP chemotherapy regimen, do not have any sperm in the ejaculate after one year.

b. Bone marrow transplantation for cancer of nonmalignant diseases usually require prior irradiation and chemotherapy. This is associated with high risk (85%) of complete failure of sperm production.

c. Connective tissue / autoimmune diseases as lupus and

rheumatoid arthritis requiring treatment with chemotherapy.

d. Genetic abnormalities associated with rapid loss of male germ cells e.g. Kleinefelter syndrome, Y chromosome microdeletion (AZFc).

Methods used for Fertility Preservation

Methods used to preserve fertility in men are generally divided into two categories:

Protection of the testes from damage caused by cancer treatment:

1. Shielding the testes from radiation field.

2. Protection of the testes from the effect of chemotherapy.

GnRH agonists are a group of medications that suppress the master gland in the brain, preventing the release of the hormones that stimulate sperm production in the testes. Although suggested, there is no proof that they actually increase the odds for pregnancy after the use of chemotherapy. Actually, there is no effective protective medication available for use in men or women.

Low Temperature Storage of Sperm and Testicular Tissue:

a. Sperm Cryopreservation. This is the standard method for preservation of fertility in men. A sperm sample is obtained by masturbation and frozen for later use. If feasible multiple samples are obtained. In the future, sperm sample are used for intrauterine insemination or IVF / intracytoplasmic sperm injection (ICSI). Banking sperm was found to offer not only a chance to father children in the future but also encouragement and improved morale during disease treatment especially if it was initiated by the patient own initiative.

Lack of information and counseling is the most important reason why men diagnosed with cancer do not bank their sperm.

Although freezing may reduce the quality of sperm especially if it was not optimal before freezing, modern reproductive medicine can handle the majority of compromised specimens yielding excellent pregnancy rates, similar to those of fresh sperm.

b. Testicular Sperm Extraction (TESE). This surgical procedure retrieves sperm from inside the testes if no sperm was found in the ejaculate. If this procedure is used before cancer treatment, sperm are retrieved in over 50% of cases. Sperm or testicular biopsies are frozen for later use. ICSI is used for fertilization. In case of testicular cancer, sperm retrieval can be performed at the same time of surgery for cancer.

c. Testicular Tissue or Germ Cell Freezing. This is an experimental technique. Immature germ cells or testicular pieces are frozen for later transplantation. No pregnancy was achieved using this method so far.

In conclusion, fertility-sparing strategy is readily available to the majority of men at risk for diminished fertility through sperm cryopreservation. Men interested in fathering children in the future should be counseled about this option.