Fact Sheet

Male Fertility

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Summary

Inability to conceive a child after 6 months of unprotected sex in the absence of female causes A total sperm count less than 5 million per mL   The presence of greater than 90% abnormal sperm. Motility less than 10%. Inability of sperm to impregnate egg as determined by the post-coital test. Positive anti-sperm antibodies. Infection present.

General Considerations

In the United States it is estimated that as many as 15% of all couples have difficulty conceiving a child. In about one-third of the cases of infertility, it is man who is responsible; in another one-third, both male and female are responsible; and in another one-third, it is the female who is responsible. Current estimates suggest about 6% of men between the ages of 15 and 50 are infertile.[1]

Most causes of male infertility reflect an abnormal sperm count or quality. Although it only takes one sperm to fertilize an egg, in an average ejaculate a man will eject nearly 200 million sperm. However, because of the natural barriers in the female reproductive tract only about 40 sperm will ever reach the vicinity of an egg. There is a strong correlation between the number of sperm in an ejaculate and fertility.

In about 90% of the cases of a low sperm count the reason is deficient sperm production.

Unfortunately, in about 90% of cases, the cause for the decreased sperm formation cannot be identified and the condition is labeled "idiopathic oligospermia or azoospermia."[2] Oligospermia means a low sperm count while azoospermia is defined as a complete absence of living sperm in the semen.

Other causes of male infertility include ductal obstruction, ejaculatory dysfunctions, and infections or disorders of accessory glands.

Table 1. Causes of Male Infertility

Deficient sperm production
Ductal obstruction
Congenital defects
Postinfectious obstruction
Cystic fibrosis
Vasectomy
Ejaculatory dysfunction
Premature ejaculation Retrograde ejaculation
Disorders of accessory glands
Infection Inflammation Antisperm antibodies
Coital disorders
Defects in technique
Premature withdrawal
Erectile dysfunction

Since the overwhelming majority of men who are infertile suffer from deficient sperm production, this will be the major focus of this chapter.

Review of Male Sexual System

The male sexual system is composed of the scrotal sac, testes, genital ducts, accessory glands, and penis. The scrotal sac performs an important role in maintaining the testes at a temperature about 2^{o} C below the temperature of the internal organs so that sperm formation can occur. The cremasteric muscles help maintain the appropriate scrotal temperature by pulling the testes close to the body when they get too cold and dropping them loose when the temperature rises too high. In addition to serving the function as the location for sperm formation, the testes are also responsible for hormonal output.

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Each testicle is surrounded by a thick, sturdy capsule of connective tissue known as the tunica albuginea which serves as a protective shield for this somewhat exposed organ. Inside the testis are about 250 compartments known as testicular lobules with each lobule being composed of 1 to 4 tubules called seminiferous tubules. Each tubule is 1.5 to 2 feet long if straightened out.

Inside the seminiferous tubule sperm formation takes place with the aid of nutrient-providing cells called Sertoli cells. Sertoli cells are known to have at least 4 main functions: (1) the support, protection, and nutritional regulation of the developing sperm; (2) the breaking down of cellular debris cast off by developing sperm; (3) the secretion of a fluid that is utilized for sperm transport; and (4) the excretion of estrogen and a binding protein for testosterone

The seminiferous tubules are immersed in a web of blood and lymphatic vessels, loose connective tissue, nerves, and Le-ydig cells. These cells are responsible for the production and secretion of testosterone. Leydig cells are almost nonexistent in the testes during childhood, but are numerous and quite active in the newborn male infant and in the adult male after puberty, the two times when the testes secrete large quantities of testosterone.

The fully developed sperm (spermatozoa) is produced via a process known as spermatogenesis. Sperm production usually begins around puberty as a result of the release of the pituitary hormones leutinizing hormone (LH) and follicle stimulating hormone (FSH). LH stimulates the Leydig cells to produce testosterone while FSH stimulates the Sertoli cells to produce sperm. Other hormones are also critical, especially testosterone, which is essential for the growth and division of the germinal cells in the production of sperm. Estrogens, formed from testosterone by the Sertoli cells, are also critical to sperm function.

Genital Ducts: The genital ducts function by transporting the sperm produced in the testis out of the body. The first passage way is the epididymis, one long, highly tortuous tube about 20 feet in length. As the sperm make the passage through the epididymis, they begin to mature. After being in the epididymis for 18 to 24 hours, the sperm become more motile (inhibitory fluids secreted by the epididymis prevents full motility until after ejaculation).

From the epididymis, the sperm travel up through the duc-tus (vas) deferens, a straight tube with thick walls. Before the vas penetrates the prostate it dilates forming a region known as the ampulla. At the final portion of the ampulla, the seminal vesicles join. Upon entering the prostate, the duct is called the ejaculatory duct before it empties into the urethra.

Accessory Glands: It was previously thought that the sperm was stored in the seminal vesicles, hence their name. We now know the primary function of the seminal vesicles is the secretion of a fluid that provide nutrients to sperm and increase sperm motility. Substances secreted by the seminal vesicles include fructose, which nourishes the sperm, and large quantities of prostaglandins and fibrinogen.

Prostaglandins are thought to aid fertilization by reacting with the mucus of the vagina and cervix to make it more receptive to sperm and possibly causing contractions in the uterus and fallopian tubes to move the sperm toward the ovaries. The fibrinogen combines with prostatic secretions to form a weak coagulate, which holds the semen together after ejaculation allowing it deeper penetra-tion into the vagina. The coagulate also limits sperm motility, but as the coagulate dissolves 15 to 20 minutes after ejaculation, the sperm become highly motile.

About 60% of the volume of semen is composed of secretions from the seminal vesicles. The remainder of the semen is composed of prostatic fluid (30% of the total volume) and secretions from the vas deferens including sperm and fluid (10% of total volume).

The prostate, a doughnut-shaped gland about the size of walnut lying below the bladder and surrounding the urethra, secretes a thin, milky, alkaline fluid which lubricates the urethra to prevent infection and increases sperm motility.

The alkaline nature of the prostatic secretion is extremely important to successful fertilization of the egg, because the fluid of the vas deferens as well as the vaginal secretions are relatively acidic. Sperm do not become optimally mobile until the pH of the surrounding fluids rises to approximately 6 to 6.5. Consequently, the prostatic fluid plays an important role in promoting sperm motility by neutralizing the acid and raising the pH of semen to 7.5.

The final accessory sexual glands are the bulbourethral glands, pea-sized formations located below the prostate and around the urethra. The bulbourethral glands produce a thin, milky secretion that lubricates the urethra and prepares the urethra for the transport of the semen.

The Penis: The penis consists primarily of erectile tissue, the urethra, and blood vessels, all surrounded externally by skin. The penis is divided into two distinct sections, the shaft and the head (glans penis). The glans is the most important source of nerve impulses to signal the sexual response.

The shaft of the penis contains erectile tissue that is housed in three cylindrical masses. Two, the corpus cavernosum, are located around central arteries and one, the corpus cavernosum or spongiosum, surrounds the urethra.

Erection is the result of dilation of the arteries in the penis combined with the filling of the erectile tissue. In simple terms,an erection requires that the volume of blood entering the penis exceed the volume leaving it. The erectile tissue is really nothing more than large, cavernous, blood storage compartments, which are normally relatively empty but which become dilated when arterial blood flows rapidly into them under pressure and the outflow if partially occluded. The erectile tissue is surrounded by a strong membrane composed of hard fibers which greatly increases the pressure within the ballooning erectile tissue, thus the penis becomes hard and elongated.

Diagnostic Considerations

Semen analysis is the most widely used test to estimate fertility potential in the male. The semen is analyzed for concentration of sperm and sperm quality. The total sperm count as well as sperm quality of the general male population has been deteriorating over the last few decades. In 1940, the average sperm count was 113 million per mL, in 1990 that value had dropped to 66 million.[3]

Adding to this problem, the amount of semen fell almost 20% from 3.4 mL to 2.75 mL. Altogether, these changes mean that men are now supplying about 40% of the number of sperm per ejaculate compared to 1940 levels.

The downward trend in sperm counts has led to speculation that environmental, dietary, or lifestyle changes in recent decades may be interfering with a man's ability to manufacture sperm. Although controversial, there is substantial evidence that supports this speculation. This evidence and methods for improving sperm quality are discussed in greater detail below methods for improving sperm quality are discussed in greater detail below.

Table 2. Possible Causes of Falling Sperm Counts

Increased scrotal temperature
Tight-fitting clothing and briefs Varicoceles are more common
Environmental
Increased pollution Heavy metals (lead, mercury, arsenic, etc.)
Organic Solvents
Pesticides (DDT, PCBs, DBCP, etc.)
Dietary
Increased saturated fats Reduced intake of fruits, vegetables, and whole grains
Reduced intake of dietary fiber Increased exposure to synthetic estrogens

In diagnosing male infertility on the basis of sperm concentration, it is important to point out that as sperm counts in the general population have declined there has also been a parallel reduction in the accepted line which differentiates between infertile and fertile men, from 40 million/mL, to 20 million/mL, to 10 million/mL, to 5 million/mL. One of the key reasons these values have dropped so drastically is that researchers are learning that quality is more important the quantity. A high sperm count means absolutely nothing if the percentage of healthy sperm is not also high.

Table 3. "Normal" Spermatogenesis

Criteria	Value
Volume	1.5-5.0 mL
Density	>20 million sperm/mL
Motility	≥30% motile
Normal forms	≥ 60%

Whenever the majority of sperm are abnormally shaped, or are entirely or relatively non-motile, a man can be infertile despite having a normal sperm concentration.

Conversely, a low sperm count does not always mean a man is infertile. Numerous pregnancies have occurred with men having very low sperm counts. For example, in studies at fertility clinics 52% of couples whose sperm counts were below 10 million/mL achieved pregnancy and 40% of those with sperm counts as low as 5 million/mL are able to achieve pregnancy.[1] Because of these confirmed successes in men with low sperm counts it is recommended that conventional semen analysis be interpreted with caution regarding the likelihood of conception and that more sophisticated functional tests should be used, especially when screening couples for *in vitro* fertilisation.

Table 4. Causes of Temporary Low Sperm Count
Increased scrotal temperature
Infections, the common cold, the flu, etc.
Increased stress
Lack of sleep
Overuse of alcohol, tobacco, or marijuana
Many prescription drugs
Exposure to radiation
Exposure to solvents, pesticides, and other toxins

Until recently, pregnancy was the only proof of the ability of sperm to achieve fertilization. Now there are several functional tests which in use. The post-coital test measures the ability of the sperm to penetrate the cervical mucus after intercourse. *In vitro* variants of this test are also available. One of the most encouraging tests is based on the discovery that human sperm under appropriate conditions can penetrate hamster eggs. It was established that fertile males exhibit a range of penetration of 10-100% and that penetration less than 10% is indicative of infertility. The hamster egg penetration test is considered to predict fertility in 66% of the cases compared to about 30% for conventional semen analysis.[1]

Table 5. Male Fertility Tests

Test	Fertility prediction accuracy
Semen analysis Hamster egg penetration	30 %

Another important test in the diagnosis of infertility is the detection of antisperm antibodies. These antibodies, when produced by the man, usually attack the tail of the sperm thereby impeding the sperm's ability to move and penetrate the cervical mucus. In contrast, the antisperm antibodies produced by women are typically directed against the head. The presence of anti-sperm antibodies in semen analysis is usually a sign of past or current infection in the male reproductive tract.

Therapeutic Considerations

Standard medical treatment of oligospermia can be quite effective when the cause is known, e.g., increased scrotal temperature, chronic infection of male sex glands, prescription medicines, and endocrine disturbances (including hypogo-nadism and hypothyroidism). However, as stated above, in about 90% of the cases of oligospermia, the cause is unknown (idiopathic oligospermia). In regards to azoospermia, if the cause is ductal obstruction, new surgical techniques are showing some good results.[1]

In the treatment of idiopathic oligospermia or azoospermia, the rational approach is to focus on enhancing those factors which promote sperm formation. In addition to scrotal temperature, sperm formation is closely linked to nutritional status. Therefore, it is critical that men with low sperm counts have optimal nutritional intake. In addition to consuming a healthful diet, there are several nutritional factors that deserve special mention: vitamin C and other antioxidants, fats and oils, zinc, folate, vitamin B_{12}, arginine, and carnitine. In addition, it appears important for men with low sperm count to avoid dietary sources of estrogens.

Some herbs, especially *Panax ginseng* and *Eleutherococcus senticosus*, are known to increase sperm counts. And finally, another popular natural treatment of male infertility involves the use of glandular therapy. The concept behind this therapy is discussed below.

Scrotal Temperature

The scrotal sac normally keeps the testes at a temperature of between 94 and 96 degrees Fahrenheit.[2] At temperature above 96^{o} F, sperm production is greatly inhibited or stopped completely. Typically, the mean scrotal temperature of infertile men is significantly higher than fertile men. Reducing scrotal temperature in infertile men will enough make them fertile.

This temperature reduction is best done by not wearing tight-fitting underwear or tight jeans, and avoiding hot tubs.

In addition, the following exercises can raise scrotal temperature, especially if a man is wearing synthetic fabrics, exceptionally tight shorts, or tight bikini underwear: rowing machines, simulated cross-country ski machines, treadmills, and jogging. After exercising, a man should allow his testicles to hang free to allow them to recover from heat buildup.

Infertile men should wear boxer-type underwear and periodically apply a cold shower or ice to the scrotum. They can also choose to use a device called a testicular hypothermia device or "testicle cooler" to reduce scrotal temperatures. Still in its somewhat primitive stage, the testicle cooler looks like a jock strap from which long, thin tubes have been extended. The tubes are attached to a small fluid reservoir filled with cold water that attaches to a belt around the waist.
The fluid reservoir is also a pump that causes the water to circulate. When the water reaches the surface of the scrotum it evaporates and keeps the scrotum cool. Because of the evaporation, the reservoir must be filled every six hours or so. It is recommended that the testicle cooler must be worn daily during waking hours. Most users claim that it is fairly comfortable and easy to conceal.[4]

Increased scrotal temperature can be due to the presence of a varicocele. A large varicocele can cause the scrotum temperatures high enough to inhibit sperm production and motility. Surgical repair may be necessary, but scrotal cooling should be tried first.

Infections and Infertility

Infections in the male genito-urinary tract including infections of the epididymis, seminal vesicles, prostate, bladder, and urethra are thought to play a major role in many cases of infertility.[5] The exact extent of the role they play is largely unknown because of the lack of suitable diagnostic criteria coupled with the asymptomatic nature of many infections. The presence of antisperm antibodies is considered to a good indicator of a chronic infection in the absence of other clinical findings.

There are a wide number of bacteria, viruses, and other organisms which can infect the male genito-urinary system. It is beyond the scope of this chapter to discuss every type of infection, therefore the discussion will be limited to *Chlamydia trachomatis*. Chlamydia is now recognized as the most common as well as the most serious of infections in the male genitourinary tract.[5]

Chlamydia is considered a sexually transmitted disease. In women, chlamydia infection can lead to pelvic inflammatory disease (PID) and scarring of the fallopian tubes. Previous chlamydia infection accounts for a large number of cases of female factor infertility. In men, chlamydia infection can lead to equally disabling effects. Chlamydia is the major cause of acute non-bacterial prostatitis and urethritis. Typically the symptoms will be pain or burning sensations upon urination or ejaculation. More serious is chlamydia infection of the epididymis and vas deferens. The resultant damage to these organs parallels the tubal damage in women. Serious scarring and blockage can occur. During an acute chlamydia infection, antibiotics are essential. Chlamydia is sensitive to tetracyclines and erythromycin. Unfortunately, because chlamydia lives within human cells it may be difficult to totally eradicate the organism with antibiotics alone.

While acute chlamydial infections are usually associated with severe pain, chronic infections of the urethra, seminal vesicles, or prostate can go on with little or no symptoms. It is estimated that 28% to 71% of infertile men have evidence of a chlamydial infection.[5]

Because of the possible link between chlamydia and low sperm counts, there have been several double-blind studies on the effects of antibiotics on sperm counts. These studies have shown only limited improvements in sperm count and sperm quality.[5]

However, there have been isolated cases of tremendous increases in sperm counts and sperm quality after antibiotic treatment. If electing this form of treatment, both partners should take the antibiotic. However, it should be used only if there is reason to believe a chronic infection is present and after the recommendations given in Chapter VI:Epi-didymitis has been employed for at least 3 months. The presence of antisperm antibodies may indicate a chronic chlamydia infection. In the absence of a positive culture, rectal ultrasonagraphy and the detection of antibodies directed against chlamydia can confirm the diagnosis.

Avoiding Estrogens

According to experts on the impact of the environment and diet on fetal development, we now live in an environment that can be viewed as "a virtual sea of estrogens."[6,7] Increased exposure to estrogens during fetal development as well as during the reproductive years is suggested to be a major cause of the tremendous increase in the disorders of development and function of the male sexual system.

The relationship between estrogens and male sexual development is best viewed by examining the effects of the synthetic estrogen, diethylstilbesterol (DES). Between 1945 and 1971 several million women were treated with DES. By 1970, the side effects of DES became more known. DES is now recognised to have led to substantial increases in the number of men suffering from developmental problems of the reproductive tract as well as decreased semen volume and sperm counts.[5] As well as being used in humans, DES and other synthetic estrogens were used for 20-30 years in the livestock industry to fatten the animals and help them grow faster.

Although many synthetic estrogens like DES are now outlawed, many livestock and poultry are still hormonally mnipulated, especially dairy cows. Cow's milk contains substantial amounts of estrogen due to modern farming techniques. The rise in dairy consumption since the 1940s inversely parallels the drop in sperm counts. Avoidance of hormone-fed animal products and milk products are important for male sexual vitality, especially in men with low sperm counts or testosterone levels.

There are reports that estrogens have been detected in drinking water.[6,7] Presumably the estrogens are recycled from excreted synthetic estrogens (birth control pills) at water treatment plants. These estrogens may be harmful to male sexual vitality as they are more potent since they do not bind to sex-hormone-binding-globulin (SHBG). Purified or bottled water may be a suitable option to prevent exposure.

There are other sources of estrogen from the environment (food, water, and air) that can weaken male sexual vitality. For example, many of the chemicals that we have contaminated our environment with in the past 50 years are weakly estrogenic. Most of these chemicals, like PCBs, dioxin, and DDT, are resistant to biodegradation and are recycled in our environment until they find safe haven in our bodies.

For example, even though DDT has been banned for nearly 20 years, it is still often found in the soil and root vegetables such as carrots and potatoes.

These toxic chemicals are known to interfere with sper-matogenesis, but more important may be their effects during sexual development. All of the estrogenic factors discussed above are thought to have their greatest impact during fetal development. Based on animal studies, these estrogens inhibit the multiplication of the Sertoli cells. The number of Sertoli cells is directly proportional to the amount of sperm that can be produced as each Sertoli cell can only support a fixed number of germ cells that will develop into sperm.

Sertoli cell multiplication occurs primarily during fetal life and before puberty. It is controlled by follicle stimulating hormone (FSH). In animal studies, estrogens administered early in life inhibit FSH secretion resulting in reduced number of Sertoli cells and, in adult life, reduced sperm counts. Evidence exists to indicate that the same events occur in humans.[6] The best example are the sons of women exposed to DES during pregnancy who, like the animals exposed to estrogens, show reduced sperm counts. Even if a mother didn't take DES she may have followed the typically low-fiber, high-fat diet of most Americans. Such a diet is associated with higher levels of estrogens because, without the fiber, excreted estrogens are reabsorbed.

If testosterone levels are low or marginal, or if estrogen levels are elevated, a diet rich in legumes (beans), especially soy foods, may be of benefit. Soy is a particularly good source of isoflavonoids. These compounds are also known as "phytoestrogens" signifying their mild estrogenic activity. The isoflavonoids in soybeans have about 0.2% of the estrogen activity of estradiol, the principal human estrogen. Isoflavones actually bind to estrogen receptors. Their weak estrogenic action is in actuality an anti-estrogenic effect as it prevents the binding of the body's own estrogen to the receptor. In addition, phytoestrogens may reduce the effects estrogens by the body by stimulating the production of SHBG so that the estrogen is bound.[8] Soy, as well as other legumes, nuts and seeds, is also a good source of phytosterols which may aid in the manufacturer of steroid hormones including testosterone.

Nutritional Considerations

Vitamin C and Other Antioxidants: Free radical or oxidative damage to sperm is thought to be responsible for many cases of idiopathic oligospermia,[9] with high levels of free radicals found in the semen of 40% of infertile men.[13]

Three factors combine to render sperm particularly susceptible to free radical damage: (1) a high membrane concentration of polyunsaturated fatty acids; (2) active generation of free radicals; and (3) a lack of defensive enzymes. All of these factors combine to make the health of the sperm critically dependent upon antioxidants. Although most free radicals are produced during normal metabolic processes, the environment contributes greatly to the free radical load. Men exposed to increased levels of sources of free radicals are much more likely to have abnormal sperm and sperm counts.[1,9-12]

Cigarette smoking in particular is associated with decreased sperm counts and sperm motility as well as an increased frequency of abnormal sperm.[12] Cigarette smoking, as well as the increase in environmental pollution, are thought to be major contributors to the decrease in sperm counts seen in many industrialized nations during the past few decades. Sperm are extremely sensitive to free radicals because they are so dependent upon the integrity and fluidity of their cell membrane for proper function. Without proper membrane flu-idity, enzymes are activated, which can lead to impaired motil-ity, abnormal structure, loss of viability, and ultimately death to the sperm.[9] The major determinant of membrane fluidity is the concentration of polyunsaturated fatty acids, particularly omega-3 fatty acids like docosahexanoic acid, which are very susceptible to free radical damage. The sperm have a relative lack of superoxide dismutase and catalase which can prevent or repair oxidative damage. Adding to this more susceptible state is the fact that sperm generate high quantities of free radicals to help breakdown barriers to fertilization.

Antioxidants like vitamin C, beta-carotene, selenium, and vitamin E, have been shown to be very important in protecting the sperm against damage. Vitamin C plays an especially important role in protecting the sperm's genetic material (DNA) from damage. Ascorbic acid levels are much higher in seminal fluid compared to other body fluids including the blood.

When dietary vitamin C was reduced from 250 mg to 5 mg per day in healthy human subjects, the seminal fluid ascorbic acid decreased by 50% and the number of sperm with damage to their DNA increased by 91%.[14] These results indicated that dietary vitamin C plays a critical role in protecting against sperm damage and that low dietary vitamin C levels were likely to lead to infertility.

It is now well-documented that cigarette smoking greatly reduces vitamin C levels throughout the body. Even the Food and Nutrition Board, the organization which calculates the Recommended Dietary Allowances (RDAs) acknowledges that smokers require at least twice as much vitamin C compared to nonsmokers.[15] In one study, men who smoked 1 pack of cigarettes a day received either 0, 200, or 1,000 mg of vitamin C. After one month, sperm quality improved proportional to the level of vitamin C supplementation.[16]

Non-smokers also appear to benefit as from vitamin C as smokers. In one study, 30 infertile but otherwise healthy men received either 200 mg or 1,000 mg vitamin C or placebo daily.[17] There were weekly measurements of sperm count, viability, motility, agglutination, abnormalities, and immaturity. After one week, the 1,000 mg group demonstrated a 140% increase in sperm count, the 200 mg group a 112%, and the placebo group no change. After three weeks both vitamin C groups continued to improve, with the 200 mg group catching up to the improvement of the 1,000 mg group. One of the key improvements was observed in the number of agglutinated sperm. Sperm become agglutinated when antibodies produced by the immune system bind to the sperm. Antibodies to sperm are often associated with chronic genito-urinary tract or prostatic infection. When more than 25% of the sperm are agglutinated fertility is very unlikely.

At the beginning of the study all three groups had over 25% agglutinated sperm, after three weeks only 11% of the sperm in the vitamin C groups were agglutinated. Although this result is significant, the most impressive result of the study was that at the end of 60 days, all of the vitamin C group had impregnated their wives, compared to none for the placebo group. It can be concluded from these results that vitamin C supplementation can be very effective in treating male infertility, particularly if the infertility is due to antibodies against sperm.

Other dietary antioxidants, like vitamin E, selenium, and beta-carotene are also important and should be supplemented. Vitamin E supplementation appears especially warranted as it is the main antioxidant in various cell membranes, including sperm membranes. Vitamin E has been show to play an essential role in inhibiting free radical damage to the unsaturated fatty acids of the sperm membrane.[18] In addition, vitamin E has been shown to enhance the ability of sperm to fertilize an egg in test tubes. Although vitamin E supplementation at a 300 IU per day has not been shown to improve sperm counts or motility,[19] supplementation appears to be indicated based on its physiological effects alone. Vitamin E may prove to exert more beneficial effects on sperm counts or motility when given at higher levels (600-800 IU per day).

Sperm are also particularly susceptible to the damaging effects of heavy metals like lead, cadmium, arsenic, and mercury. A hair mineral analysis for heavy metals should be performed on all men with reduced sperm counts to rule out heavy metals as a cause.

Fats and Oils: Considering the effects of fats and oils on agglutination and cell membrane dynamics, certain fats are best avoided in infertile men while others should be increased. Saturated fats, hydrogenated oils, trans-fatty acids, and cotton, coconut and palm oil should be avoided. Coconut and palm oils are primarily saturated fat while cotton seed may contain toxic residues, due to the heavy spraying of cotton and its high levels of gossypol, a substance known to inhibit sperm function.

In fact, gossypol is being investigated as the "male birth control pill." Its use as an anti-fertility agent began after studies demonstrated that men who had used crude cotton seed oil as their cooking oil were shown to have low sperm counts followed by total testicular failure.[20] Excessive consumption saturated fats combined with inadequate intake of essential fatty acids will change the fatty acid composition of the sperm membranes thus decreasing fluidity and interfering with sperm motility. The patient must be informed to read food labels carefully and avoid all sources of cotton seed oil and other damaging oils.

While the intake of saturated and hydrogenated fats must be eliminated, the intake of polyunsaturated oils should be increased. These oils function in all aspects of sexual function including sperm formation and activity.

Zinc: Zinc is perhaps the most critical trace mineral for male sexual function. It is involved in virtually every aspect of male reproduction including the hormone metabolism, sperm formation, and sperm motility.[21]

Among many other things, zinc deficiency is characterized by decreased testosterone levels and sperm counts. Zinc levels are typically much lower in infertile men with low sperm counts indicating that a low zinc status may be the contributing factor to the infertility.

Several studies have been designed to measure the effect of zinc supplementation on sperm counts and motility.[22-24] The results from all of the studies support the use of zinc supplementation in the treatment of oligospermia especially in the presence of low testosterone levels. The effectiveness of zinc is best illustrated by a study in 37 men with infertility of greater than 5 years duration whose sperm counts were less than 25 million/mL.[24]

Blood testosterone levels were also measured. The men received a supplement of zinc sulfate (60 mg elemental zinc daily) for 45-50 days. In the 22 patients with initially low testosterone levels, mean sperm count increased significantly from 8 to 20 million. Testosterone levels also increased and 9 out of the 22 wives became pregnant during the study. This result is quite impressive given the long-term nature of the infertility and the rapidity of the results. In contrast, in the 15 men with normal testosterone levels, although sperm count increased slightly, there was no change in testosterone level and no pregnancies occurred.

Optimal zinc levels must be attained if optimum male sexual vitality is desired. Although severe zinc deficiency is quite rare in this country, many men consume a diet that does not provide the RDA for zinc (15 mg). Zinc is found in whole grains, legumes, nuts, and seeds. In addition to eating these zinc containing foods, recommending supplementary zinc (45-60 mg per day) appears warranted.

Vitamin B_{12}: Vitamin B_{12} is involved in cellular replication. A deficiency of B_{12} leads to reduced sperm counts and sperm motility. Even in the absence of a vitamin B_{12} deficiency, supplementation appears to be worthwhile in men with sperm counts less than 20 million per mL or a motility rate of less than 50%. In one study, 27% of men with sperm counts less than 20 million given 1,000 mcg per day of vitamin B_{12} were able to achieve a total count in excess of 100 million.[25] In another study, 57% of men with low sperm counts given 6,000 mcg per day demonstrated improvements.[26]

Arginine: The amino acid arginine is required for the replication of cells, making it essential in sperm formation. Ar-ginine supplementation is often, but not always, an effective treatment of male infertility. The critical determinate appears to be the level of oligospermia. If sperm counts are less than 20 million per mL, arginine supplementation is less likely to be of benefit. In order to be effective, it appears that the dosage of L-arginine be at least 4 g a day for three months. In perhaps the most favorable study, 74% of 178 men with low sperm counts had significant improvements in sperm counts and motility.[27] L-arginine therapy should be reserved for use after other nutritional measures have been tried.

Carnitine: Carnitine is essential in the transport of fatty acids into the mitochondria. A deficiency of carnitine results in a decrease in fatty acid concentrations in the mitochondria and reduced energy production.

Carnitine concentrations are extremely high in the epididymis and sperm, suggesting a role for carnitine in male reproductive function.

The epididymis derives the majority of its energy requirements from fatty acids, as do the sperm, during transport through the epididymis. After ejaculation, the motility of sperm correlates directly with car-nitine content.[28] The higher the carnitine content the more motile the sperm. Conversely, when carnitine levels are low, sperm development, function and motility are drastically reduced.

Supplementing the diet with L-carnitine may be useful in restoring male fertility in some cases. The optimal dosage is 300-1,000 mg of L-carnitine three times daily. However, be cause L-carnitine tends to be relatively expensive, the other nutritional measures should be tried first.

Botanical Medicines

Ginseng: Current scientific investigation suggests that both *Panax ginseng* (Chinese or Korean ginseng) and *Eleuthero-coccus sentiosus* (Siberian ginseng) are likely effective in the treatment of male infertility. Both botanicals have a long history of use as male "tonics." Although human clinical studies are lacking, *Panax ginseng* has been shown to promote the growth of the testes, increase sperm formation and testosterone levels, and increase sexual activity and mating behavior in studies with animals (see Chapter V:Panax Ginseng for refer-ences). Siberian ginseng has also shown some benefit to the male reproductive function in animal studies as it has been shown to increase reproductive capacity and sperm counts in bulls (see Chapter V:Eleutherococcus Senticosus for refer-ences). These results seem to support the use of either ginseng as a fertility and virility aid.

In general, *Panax ginseng* is regarded as being more potent in effects (particularly stimulant effects) than *Eleutherococcus senticosus*. Although Siberian ginseng contains no ginsenosides and is not a true ginseng, it does possess many of the same effects that *Panax ginseng* exerts, but it is generally regarded as being milder.

Pygeum Africanum: Pygeum may be effective in improving fertility in cases where diminished prostatic secretion plays a significant role. Pygeum has been shown to increase prostatic secretions and improve the composition of the seminal fluid.[29-31] Specifically, pygeum administration to men with decreased prostatic secretion has led to increased levels of total seminal fluid plus increases in alkaline phosphatase and protein. Py-geum apppears to be most effective in cases where the level of alkaline phosphatase activity is reduced (i.e., less than 400 IU/cm^3) and there is no evidence of inflammation or infection (i.e., absence of white blood cells or IgA). The lack of IgA in the semen is a good indicator of clinical success. In one study, the patients with no IgA in the semen demonstated an alkaline phosphatase increase from 265 to 485 IU/cm^3.[29] In contrast, those subjects with IgA showed only a modest increase from 213 to 281 IU/cm^3.

Pygeum extract has also shown an ability to improve the capacity to achieve an erection in patients with BPH or prosta-titis as determined by nocturnal penile tumescence in a double-blind clinical trial.[32] BPH and prostatitis are often associated with erectile dysfunction and other sexual disturbances.

Presumably, by improving the underlying condition, pygeum can improve sexual function.

Glandular Therapy
For almost as long as historic records have been kept, glandular therapy has been an important form of medicine. The basic concept underlying the medicinal use of glandular substances from animals is that "like heals like." In the case of low testosterone levels or low sperm counts, extracts of bovine (beef) orchic or testicular tissues are often recommended by physicians practicing glandular therapy.
It is well established that a number of glandular preparations are effective orally because of active hormones (e.g., thyroid, adrenal, and thymus). Presumably, orchic or testicular products may also be of benefit. Unfortunately, dosage, as well as effectiveness, may vary from one manufacturer to another.

Therapeutic Approach

Male infertility is most often due to an abnormal sperm count or semen quality. Referral to an urologist or fertility specialist for a complete evaluation including is often necessary. As elevated scrotal temperature is a common cause of infertility, scrotal cooling through the use of loose underwear made of cotton, avoidance of activities which elevate testicular temperature (e.g., hot tubs) and application of cold water to the testes should be utilized. Nutritional status should be optimized (especially anti-oxidants and zinc), environmental pollutants identified and eliminated, and fertility-enhancing botanicals such as the ginsengs consumed.

General Measures:
Maintain scrotal temperatures between 94-96^{o} F. Avoid exposure to free radicals. Identify and eliminate environmental pollutants Stop or reduce all drugs, especially anti-hypertensives, antineoplastics such as cyclophosphamide, and anti-inflammatory drugs such as sulfasalazine

Diet: Avoid dietary sources of: free radicals; saturated fats; hydrogenated oils; trans-fatty acids; and cottonseed oil. Increase consumption of: legumes, especially soy (high in phytoestrogens and phytosterols); good dietary sources of antioxidant vitamins, carotenes, and flavonoids (dark-colored vegetables and fruits); and essential fatty acids and zinc (nuts and seeds).

Recommend the daily consumption of: 8-10 servings of vegetables; 2-4 servings of fresh fruits; and 1/2 cup of raw nuts or seeds.

Nutritional Supplements:
Multiple vitamin and mineral supplement taken once a day with food

- Vitamin C – 200mg
- Vitamin E – 300 iu
- Vitamin D – 100iu
- Vitamin B1 – 20mg
- Vitamin B2 – 20mg
- Vitamin B3 – 20mg
- Vitamin B5 – 20mg
- Vitamin B6 – 20mg
- Vitamin B12 – 20mcg
- Vitamin K – 100mcg
- Vitamin A – 2300iu
- Zinc – 30mg
- Calcium – 20mg
- Manganese – 5mg
- Magnesium – 20mg
- Beta Carotene – 15mg
- Iron – 5mg
- Folic acid – 400mcg
- Selenium – 100mcg
- Chromium – 20mcg
- L-arginine - 1000mg
- L-carnitine - 100mg
- L-taurine – 100mg

Botanical Medicines:
Panax ginseng (three times per day dosages)
High quality crude ginseng root - 1.5-2 g/d 3x/d
Standardized extract (5% ginsenosides) 500mg 3x/d
The dosage of ginseng is related to the ginsenoside content. The typical dose (taken one to three times daily) should contain a saponin content of at least 25 mg of gin-senoside Rg1 with a ratio Rg1 to Rb1 of 2:1. For example, for a high quality ginseng root powder containing 5% gin- senosides, the dose would be 500 mg; for a standardized *Panax ginseng* extract containing a 18% saponin content calculated as ginsenoside Rg1, the standard dose would be 150 mg.

As each individual's response to ginseng is unique, care must be taken to observe possible ginseng toxicity It is best to begin at lower doses and increase gradually. The Russian approach for long-term administration of either *Panax* or *Siberian ginseng* is to use ginseng cyclically for a period of 15-20 days followed by a two-week interval without any ginseng.

This recommendation appears prudent.
Eleutherococcus senticosus (three times per day dosages)
Dried root - 2-4 g
Tincture (1:5) - 10-20 mL
Fluid extract (1:1) - 2.0-4.0 mL
Solid (dry powdered) extract (20:1) - 100-200 mg

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