Male Infertility: Nutritional and Environmental Considerations

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Abstract
Studies confirm that male sperm counts are declining, and environmental factors, such as pesticides, exogenous estrogens, and heavy metals may negatively impact spermatogenesis. A number of nutritional therapies have been shown to improve sperm counts and sperm motility, including carnitine, arginine, zinc, selenium, and vitamin B12. Numerous antioxidants have also proven beneficial in treating male infertility, such as vitamin C, vitamin E, glutathione, and coenzyme Q10. Acupuncture, as well as specific botanical medicines, have been documented in several studies as having a positive effect on sperm parameters. A multi-faceted therapeutic approach to improving male fertility involves identifying harmful environmental and occupational risk factors, while correcting underlying nutritional imbalances to encourage optimal sperm production and function. (Altern Med Rev 2000;5(1):28-38.)

Introduction
An estimated six percent of adult males are thought to be infertile. Infertility is defined by most authorities as the inability to achieve a pregnancy after one year of unprotected intercourse. Conception is normally achieved within 12 months in 80-85 percent of couples using no contraceptive measures; thus an estimated 15 percent of couples attempting their first pregnancy will have difficulty conceiving. While certain cases of male infertility are due to anatomical abnormalities such as varicoceles, ductal obstructions, or ejaculatory disorders, an estimated 40-90 percent of cases are due to deficient sperm production of unidentifiable origin.

Diagnosis and Evaluation
While the focus of this article is on specific nutritional and environmental factors, there are other important diagnostic considerations when evaluating male infertility. These include endocrine abnormalities, such as hyper- and hypothyroidism or hypogonadism. Prescription drugs, including phenytoin, glucocorticoids, sulfasalazine, and nitrofurantoin all may have detrimental effects on sperm production and motility. A detailed history of exposure to occupational and environmental toxins, recreational drugs and alcohol, excessive heat or radiation, and previous genitourinary infections should be elicited. Concurrent pathologies may also affect sperm production. Hepatic cirrhosis is associated with increased endogenous estrogens, which can suppress pituitary gonadotropin secretion and affect spermatogenesis. In addition, an estimated 80 percent of men with hemochromatosis have some degree of testicular dysfunction.
Scrotal temperature is highly regulated by the body, and sperm production is greatly reduced at temperatures above 96°F. Men attempting to improve their fertility should not wear tight fitting pants or underwear (boxer shorts instead of briefs), as should avoid strenuous exercise, hot tubs, and baths.

**Semen Analysis**

A normal semen sample should have a volume of 1.5-5.0 ml, with greater than 20 million sperm/ml. The number of abnormal sperm should be less than 40 percent, with greater than 30 percent of the sperm sample demonstrating proper motility. Unfortunately, conventional semen analysis is not a highly accurate predictor of fertility. Purvis et al reported, after surveying infertility clinics, that 52 percent of men with a sperm count below 20 million/ml were able to impregnate their partners and 40 percent of men with a sperm count below 10 million/ml were also able to conceive. Conventional semen analysis often fails to identify infertile males with “normal” samples and conversely fails to identify fertile males with subnormal semen parameters. Another confounding factor is variations in sperm density, motility, and morphology among multiple samples from the same subject.

More sensitive tests are available, including the post-coital test, which measures the ability of sperm to penetrate cervical mucus, and the hamster-egg penetration test, which measures the in vitro ability of sperm to penetrate hamster eggs. This test predicts fertility in an estimated 66 percent of cases, in comparison to 30 percent with conventional sperm analysis.

**Infection**

The role of infection in idiopathic male infertility has been underestimated, in particular chronic asymptomatic chlamydial infections. Chlamydia can reside in the epididymis and vas deferens, affecting sperm development and fertility. One study suggests approximately 28-71 percent of infertile men have evidence of a chlamydial infection. The presence of anti-sperm antibodies may indicate an undiagnosed infection, and is estimated to be a relative cause of infertility in 3-7 percent of cases. In a study designed to examine the effects of antioxidants on anti-sperm antibodies, there was a significant correlation between beta carotene levels and antibody titers, suggesting dietary antioxidants are involved in mediating immune function in the male reproductive system.

**Declining Sperm Counts**

There is a growing body of scientific evidence supporting the idea that sperm counts have declined considerably over the last 50 years. Carlsen et al analyzed a total of 61 studies including 14,947 men from the years 1938 to 1991, for mean sperm density and mean seminal volume. Their results show a significant decline in mean sperm density from 113 million/ml in 1940 to 66 million/ml in 1990 (p<0.0001). Seminal volume decreased from an average of 3.40 ml to 2.75 ml (p=0.027). This demonstrates a 20-percent drop in volume and a substantial 58-percent decline in sperm production in the last 50 years. Three other recent reports also found semen quality has declined among donors over the last 20 years. Because the decline in sperm production is relatively recent, one must suspect a combination of environmental, lifestyle, and dietary factors might be interfering with spermatogenesis.

**Environmental Risk Factors**

Current evidence suggests there may be environmental reasons for deteriorating sperm quality, including occupational exposure to various chemicals, heat, radiation, and heavy metals. In addition, exposure to environmental estrogens and pesticides has been
linked to alterations in spermatogenesis. Lifestyle risk factors are also significant, including cigarette smoking, alcohol consumption, chronic stress, and nutritional deficiencies.13

Xeno-Estrogens and Pesticides

Increased exposure to estrogens is thought to be responsible for not only prenatal testicular damage, but may also contribute to post-natal depression of testicular function and spermatogenesis. Exogenous estrogens impact fetal development by inhibiting the development of Sertoli cells, which determine the lifelong capacity for sperm production.

Circulating estrogens also inhibit enzymes involved in testosterone synthesis and may directly affect testosterone production.

The synthetic estrogen, diethylstilbestrol (DES), is a well-documented example of this problem. DES was prescribed from 1945 to 1971 to millions of women during pregnancy. Male offspring from those women had a higher incidence of developmental problems of the reproductive tract, as well as diminished sperm volume and sperm count.5

Synthetic estrogens are still widely used in the livestock, poultry, and dairy industries. Men wishing to improve their fertility and sperm quality probably should avoid hormone-containing dairy products and meats and opt instead for organic or hormone-free foods.

Many commonly-used pesticides, such as organochloride compounds, have estrogenic effects within the body. Chemicals such as dioxin, DDT, and PCBs are known to interfere with spermatogenesis. One study which examined the effect of DDT on male rat sexual development found low levels of DDT caused degeneration in sperm production, a decrease in the total number of sperm, and a reduced number of Leydig cells. The authors hypothesize that DDT acts as an hormonal disrupter, damaging the seminiferous epithelium and lowering local testosterone levels.14

Dietary and Lifestyle Factors

In addition to avoiding exogenous estrogens and pesticides, there are other dietary factors to consider. Adequate intake of essential fatty acids is important to ensure proper membrane fluidity and energy production in sperm cells. High dietary intake of hydrogenated oils, particularly cottonseed oil, has been shown to have a negative impact on sperm cell function. Not only does cottonseed oil contain toxic pesticide residues, it also contains high levels of the chemical gossypol, which can interfere with spermatogenesis.15

In Nigeria, a randomized, controlled trial was designed to evaluate the effect of dietary aflatoxin on infertile men. Forty percent of the 50 infertile men in the study had aflatoxin in their semen samples, compared to eight percent of the fertile control group. Infertile men exposed to dietary aflatoxin had a 50-percent higher number of abnormal sperm than controls.16

Heavy Metals

Another environmental concern with infertility is the toxic effects of heavy metals on sperm quality and production. In Hong Kong, infertile males were found to have approximately 40-percent higher hair mercury levels than fertile males of similar age.17 Occupational exposure to lead has been shown to cause a significant decrease in male fertility.18 Considering the occupational and environmental prevalence of heavy metals and their potentially negative interactions with the neuroendocrine system, a hair analysis should be included in the diagnostic work-up of idiopathic male infertility.

Cigarette Smoking

Cigarette smoking has been associated with decreased sperm count, alterations in motility, and an overall increase in the number of abnormal sperm.19 A study designed to evaluate seminal zinc levels in smokers and
non-smokers found that although smokers did not have significantly lower zinc levels than non-smokers, seminal cadmium levels were significantly increased, especially in those smoking more than one pack per day.20 Experimental evidence also suggests nicotine can alter the function of the hypothalamic-pituitary axis, affecting growth hormone, cortisol, vasopressin, and oxytocin release, which then inhibits the release of luteinizing hormone (LH) and prolactin.21 Cigarette smokers were also shown to have higher levels of circulating estradiol and decreased levels of LH, follicle-stimulating hormone (FSH), and prolactin than non-smokers, all of which potentially impact spermatogenesis. Smokers with low prolactin levels also demonstrated defects in sperm motility.22

Nutritional Therapies

Carnitine

The main function of carnitine in the epididymis is to provide an energetic substrate for spermatozoa. Carnitine contributes directly to sperm motility and may be involved in the successful maturation of sperm.23 This is especially important since epididymal sperm use fatty acid oxidation as their main source of energy metabolism, and thus tend to concentrate carnitine while in the epididymis, as carnitine is necessary for transport of fatty acids into the mitochondria.24 Low levels of carnitine reduce fatty acid concentrations within the mitochondria, leading to decreased energy production and potential alterations in sperm motility.

In a study involving 124 infertile patients, a direct correlation between semen carnitine content and sperm motility was found. The results also show a positive correlation between free L-carnitine and both sperm count and the number of motile sperm per milliliter (P<0.01).25 In one multi-center trial, 100 patients received 3 g/day of oral L-carnitine for four months. Sperm parameters were assessed before, during, and after the study. Motility was determined by computer-assisted sperm analysis. The results clearly demonstrate carnitine has a positive effect on sperm motility. The percentage of motile spermatozoa increased from 26.9±1.1 to 37.7±1.1 percent. The percent of sperm with rapid linear progression increased from a baseline of 10.8 percent to 18.0 percent. Not only did carnitine significantly affect sperm motility, but the total number of spermatozoa per ejaculate also increased.26

Another clinical study reported similar results with 3 g carnitine given daily for three months. Thirty-seven of the 47 participants had increases in sperm motility, rapid linear progression, and total number of sperm.27

In a related study, 20 men with idiopathic asthenospermia (defective sperm motility) were given acetylcarnitine, 4 g/day for 60 days. While acetylcarnitine did not affect sperm density or total motility, it did significantly increase progressive linear sperm motility. It is interesting to note that gains in sperm motility were sustained in 12 of the subjects during the four-month follow-up period. Five pregnancies occurred during treatment, with two more occurring during the four months following the trial.28

Potential Contributing Factors in Male Infertility

- Infection
- Hormonal imbalances
- Hepatic cirrhosis
- Infection
- Excessive heat
- Radiation exposure
- Heavy metal toxicity
- Cigarette smoking
- Xeno-estrogen exposure
- Pesticide exposure
- High intake of cottonseed oil
Arginine

The amino acid arginine is a biochemical precursor in the synthesis of putrescine, spermidine, and spermine, which are thought to be essential to sperm motility. In 1973, Schachter et al published a study in which arginine was given to 178 men with low sperm count. Seventy-four percent of the subjects had significant improvement in sperm count and motility after taking 4 g/day for three months.29

More recently, researchers in Italy evaluated the clinical efficacy of arginine in 40 infertile men. All the men had a normal number of sperm (> 20 million/ml) but had decreased motility which was not due to immunological disorders or infections. Subjects were given 80 ml of a 10-percent arginine HCl solution for six months. Arginine supplementation significantly improved sperm motility without any side effects.30

Zinc

Zinc is a trace mineral essential for normal functioning of the male reproductive system. Numerous biochemical mechanisms are zinc dependent, including more than 200 enzymes in the body.31 Zinc deficiency is associated with decreased testosterone levels and sperm count. An adequate amount of zinc ensures proper sperm motility and production. Zinc levels are generally lower in infertile men with diminished sperm count, and several studies have found supplemental zinc may prove helpful in treating male infertility.32

In one trial, the effect of zinc supplementation on testosterone, dihydrotestosterone, and sperm count was studied. Thirty-seven patients with idiopathic infertility of more than five-years duration and diminished sperm count received 24 mg elemental zinc from zinc sulfate for 45-50 days. The results were dramatic in the 22 subjects with initially low testosterone levels; a significant increase in testosterone levels and sperm count (from 8 to 20 million/ml) was noted, along with nine resulting pregnancies.33

Fourteen infertile males with idiopathic oligospermia were supplemented with 89 mg zinc from oral zinc sulfate for four months. Serum zinc levels were unaffected, but seminal zinc levels significantly increased. There were also improvements in sperm count and in the number of progressively motile and normal sperm. Three pregnancies occurred during the study.34

Zinc supplementation appears warranted in the treatment of male infertility, especially in cases of low sperm count or decreased testosterone levels.

Antioxidants

Polyunsaturated fatty acids and phospholipids are key constituents in the sperm cell membrane and are highly susceptible to oxidative damage. Sperm produce controlled concentrations of reactive oxygen species, such as the superoxide anion, hydrogen peroxide, and nitric oxide, which are needed for fertilization; however, high concentrations of these free radicals can directly damage sperm cells.35 Disruption of this delicate balance has been proposed as one of the possible etiologies of idiopathic male infertility.

Vitamin C

Studies have shown the concentration of ascorbic acid in seminal plasma directly reflects dietary intake, and lower levels of vitamin C may lead to infertility and increased damage to the sperm’s genetic material.36 Fraga et al demonstrated this by reducing ascorbic acid intake in healthy men from 250 mg to 5 mg per day. Seminal plasma levels of vitamin C decreased by 50 percent, with a concomitant 91-percent increase in sperm with DNA damage.37

Cigarette smoking has been documented as having deleterious effects on sperm quality. In a University of Texas study on vitamin C and sperm quality in heavy
smokers, 75 men were divided into three supplementation groups; one was given placebo, the other groups received 200 mg or 1000 mg ascorbic acid. While the placebo group showed no improvement, the ascorbic acid groups showed significant improvement in sperm quality, with the greatest improvement occurring in the 1000 mg group.38

In perhaps one of the best studies on vitamin C and male infertility, 30 infertile but otherwise healthy men were given a placebo, 200 mg, or 1000 mg vitamin C daily. After one week, the group receiving 1000 mg/day had a 140-percent increase in sperm count, while there was no change in the placebo group. The 200 mg/day group had a 112-percent increase in sperm count, while both groups demonstrated significant reductions in the number of agglutinated sperm. Most importantly, by the end of the 60-day study every participant in the vitamin C group had impregnated their partner, while no pregnancies occurred in the placebo group.39

Vitamin E

Vitamin E is a well-documented antioxidant and has been shown to inhibit free-radical-induced damage to sensitive cell membranes.40 In one study, lipid peroxidation in the seminal plasma and spermatozoa was estimated by malondialdehyde (MDA) concentrations. Oral supplementation with vitamin E significantly decreased MDA concentration and improved sperm motility, resulting in a 21-percent pregnancy occurrence during the study.41

In one randomized, cross-over, controlled trial, 600 mg/day vitamin E improved sperm function in the zona binding assay, therefore enhancing the ability of the sperm to penetrate the egg in vitro.42

Nine men with low sperm count and alterations in sperm motility were given vitamin E with the antioxidant trace mineral selenium for six months. Compared to the baseline pre-supplementation period of four months, the combination of vitamin E and selenium significantly increased sperm motility and the overall percentage of normal spermatozoa.43

Glutathione/Selenium

Glutathione is vital to sperm antioxidant defenses and has demonstrated a positive effect on sperm motility.44-46 Selenium and glutathione are essential to the formation of phospholipid hydroperoxide glutathione peroxidase, an enzyme present in spermatids which becomes a structural protein comprising over 50 percent of the mitochondrial capsule in the mid-piece of mature spermatozoa. Deficiencies of either substance can lead to instability of the mid-piece, resulting in defective motility.47,48

Glutathione therapy was used in a two-month, placebo-controlled, double-blind, cross-over trial of 20 infertile men. The subjects were given either a daily 600 mg intramuscular injection of glutathione or an equal volume of placebo. Glutathione demonstrated a statistically significant effect on sperm motility, especially increasing the percentage of forward motility.49

Sixty-nine infertile Scottish men were given either placebo, selenium, or selenium in combination with vitamins A, C, and E for three months. At the end of the trial, both selenium-treated groups had significant improvements in sperm motility; however, sperm density was unaffected. Eleven percent of the participants in the treatment groups impregnated their partner during the course of the study.50

Another study compared the effects of selenium supplementation in 33 infertile men. They were given either a 200 mcg/day dose of selenium from sodium selenite or a selenium-rich yeast for 12 weeks. While selenium concentration in seminal fluid was increased in both groups, it was markedly higher in the
yeast-Se group. Yeast-Se significantly increased glutathione peroxidase activity in the seminal fluid, but failed to produce any improvements in sperm count, motility, or morphology.51

Coenzyme Q-10

In sperm cells, coenzyme Q10 (CoQ10) is concentrated in the mitochondrial mid-piece, where it is involved in energy production. It also functions as an antioxidant, preventing lipid peroxidation of sperm membranes. When sperm samples from 22 asthenospermic men were incubated in vitro with 50 microM CoQ10, significant increases in motility were observed. CoQ10 (60 mg) was given to 17 infertile patients for a mean 103 days, and although there were no significant changes in standard sperm parameters, there was a significant improvement in fertilization rate (p<0.05).52

In another study, 10 mg/day of coenzyme Q7 (an analog of CoQ10) was given to infertile men, with resulting increases in sperm count and motility.53

Clearly, additional studies will be needed to evaluate the possible role of coenzyme Q10 in the treatment of male infertility.

Vitamin B12

Vitamin B12, in its various forms, has been studied for its effect on male infertility. Vitamin B12 is important in cellular replication, especially for the synthesis of RNA and DNA, and deficiency states have been associated with decreased sperm count and motility.

Methylcobalamin (1,500 mcg/day) was given to a group of infertile men for a period of 8-60 weeks. They were evaluated periodically by semen analysis, and standard sperm parameters were increased by 60 percent.54 In another methylcobalamin study, 1,500 mcg/day was given to 26 infertile men for a period of 4-24 weeks. Sperm analysis was conducted eight weeks into the study. Sper数 concentration increased in 38.4 percent of the cases and total sperm count increased in 53.8 percent of the men. Sperm motility increased in 50 percent of the participants. Serum LH, FSH, and testosterone levels were unchanged.55 When 6000 mcg/day was given to men with low sperm count, it resulted in a 57-percent improvement.56 Vitamin B-12 (1000 mcg/day) was administered to men with a sperm count less than 20 million/ml. By the end of the study, 27 percent of the men had a sperm count over 100 million/ml.57

Acupuncture and Botanical Medicine

Several studies have investigated the use of acupuncture as a therapy for male infertility. In one prospective controlled study, 16 infertile males were treated with acupuncture twice per week for five weeks. Compared to the control group, patients receiving acupuncture had increases in total functional sperm fraction, percentage of viability, total motile sperm per ejaculation, and overall integrity of the axonema (p<0.05).58

An additional study reported when acupuncture was performed on 28 infertile men, all sperm parameters significantly improved, with the exception of ejaculate volume.59

Ginseng has historically been used in Chinese medicine as a male Qi tonic. Panax ginseng and Eleutherococcus senticosus (Siberian ginseng) have a long history of traditional use and were commonly prescribed to enhance male virility and fertility.

Ginseng, an adaptogenic herb, has a multitude of physiological effects within the body. Chen et al found extracts of Panax
notoginseng were capable of significantly enhancing in vitro sperm motility.\textsuperscript{60} Other studies have shown that Panax ginseng promotes increased sperm formation and testosterone levels in animals.\textsuperscript{61,62}

Researchers in Korea have recently determined that administering Panax ginseng extract to animals can enhance erectile capacity and protect against atrophy and testicular damage induced by dioxin.\textsuperscript{63,64}

When 18 water extracts of Chinese medicinal herbs were evaluated for their effect on sperm motility, Astragalus was the only herb with a significant stimulatory effect. At 10 ml/mg, in vitro sperm motility was increased 146.6 ± 22.6 percent compared to control.\textsuperscript{65}

The herb Pygeum africanum may also be an effective therapy for male infertility, especially in cases of diminished prostatic secretions. Pygeum extracts have been shown to increase alkaline phosphatase activity, which helps maintain the appropriate pH of seminal fluid, and increases total prostatic secretions. Sperm motility is partly determined by the pH of the prostatic fluid. If Pygeum can raise the pH of prostatic fluid, it may have a role in promoting and maintaining optimal sperm motility.\textsuperscript{66-68}

**Conclusion**

Male infertility is a multifactorial disease process with a number of potential contributing causes. Considering the majority of male infertility cases are due to deficient sperm production of unknown origin, environmental and nutritional factors must be evaluated. Occupational risk factors, including exposure to heat, chemicals, and heavy metals needs to be examined. Lifestyle and dietary choices, pesticide residues, and xeno-estrogens all may adversely affect spermatogenesis.

Various nutritional strategies have been presented which have a beneficial impact on sperm count, motility, and ultimately, fertility. Spermatogenesis is an energetically-demanding process which requires an optimal intake of antioxidants, minerals, and nutrients.

Is it purely coincidence that sperm quality has diminished over the last 50 years, while ever increasing amounts of synthetic chemicals and hormones have been introduced to the environment and food supply? Perhaps we should consider decreased fertility in men as a physiological early warning system, a “canary in the coal mine,” so to speak, which is acting as a sensitive indicator of environmental disruptions and nutritional imbalances.

**References**


