Delaware Valley Institute of Fertility & Genetics

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THE MALE FACTOR Current approaches to understanding and treating male infertility. By George S. Taliadouros, M.D. and Kimberly B. Gleason, Ph.D.

It is generally accepted today that male factor accounts for more than 40 percent of the sources of infertility. This has given increasing impetus to more intensively study male reproductive physiology in order to provide answers to many pressing questions. In the past, most of the emphasis was placed on results from the semen analysis, part of the male's standard infertility work-up. Although there is some debate over what exactly is considered "normal," the semen analysis remains one of the primary tests used to guide decisions about treatment options for couples. Based on its results, the physician may recommend that the couple undergo some form



of Assisted Reproductive Technology (ART), such as in vitro fertilization (IVF). Today, however, there is a trend to not just overcome male factor infertility with advanced technologies, but to understand, interpret, and treat (if possible) the cause of the problem.

The semen analysis determines a man's sperm count, motility (percentage of moving sperm), and morphology (shape of the sperm) scores, which are then compared to suggested "normal" ranges established by the World Health Organization. If the results show a severe reduction in any of these parameters, the patient is considered for IVF. But in about half of the cases an assisted method of fertilization known as intracytoplasmic sperm injection (ICSI) also is recommended.

Introduced to IVF about a decade ago, ICSI has been invaluable in providing couples with severe male factor infertility the chance of conceiving, when this would otherwise not have been possible. Regardless of sperm count, motility, or morphological score, a single normal sperm can be isolated from an ejaculate and injected directly into an egg during the ICSI procedure. Therefore, the clinical approach to *treating* men with a low sperm count, motility, or morphology has been IVF/ICSI, which in fact is really not a treatment.

Now with increasing publicity on the minimal negative side effects of ART, some researchers have reverted back to evaluating the male more intensively. Male fertility can be affected by numerous factors, including environmental or genetic influences. The good news is that many environmental factors can be overcome with supplements such as multi-vitamins and minerals, dietary changes, and lifestyle changes.

For example, a recent article published in the March 2002 issue of the medical journal Fertility and Sterility mentions that men can boost the quality of their sperm by supplementing their diets with folic acid and zinc. The researchers found that subfertile men who received the nutritional supplements for about six months exhibited a 74 percent increase in the number of normally formed sperm in their ejaculates.

Another article found in the January 2002 issue of *Working Mother* magazine discusses how men can boost their fertility by limiting their intake of foods containing partially hydrogenated oils, chemical pesticides, and saturated fats.

The authors suggest that men who are attempting to conceive should instead eat more nuts and white meat or fish, which are all high in amino acids (arginine, L-carnitine, B12) that

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promote sperm production and boost sperm motility. They should also eat more citrus fruits, which supply vitamin C, and more organic dark leafy vegetables, which are excellent sources of folic acid. Vitamin C also is a potent antioxidant, and folic acid is known to be beneficial against neural tube damage in developing fetuses.

Genetic factors that can affect male fertility cannot always be treated, but they can be identified so that the patient can be properly counseled on realistic expectations and outcomes. With current technologies in molecular biology and genetics, we have come to realize that approximately 30 percent of men with infertility problems have an underlying genetic disorder. Some of these disorders may be suspected after results of a semen analysis are obtained or after a physical examination is conducted.

"Genetic scientists hope to identify specific genes that affect infertility and to possibly correct aberrations with gene therapy techniques."

For example, men who have no sperm in their ejaculates can often be identified as carriers of cystic fibrosis, a condition that can result in absence of the vas deferens (a means by which sperm are ejaculated). Likewise, a physical examination may lead to the diagnosis of the most common male chromosomal aberration, Klinefelter's syndrome. Approximately 1 in 700 to 1,000 men (5 percent of infertile men) have this disorder, which is often characterized by small testes, degenerative regions of the testes, functional impairment of sperm support cells, and development of male breasts. Patients who have these conditions should be aware that they might be able to conceive with the aid of ART, but that they risk transferring these problems to their offspring.



Many genetic disorders can, in turn, exist without outward signs. Close to 8 percent of couples that undergo IVF for male factor infertility may have structural chromosomal disorders that can be identified only by routine DNA analysis techniques. These defects may involve deletions of or harmful recombinations of DNA material on one or several critical regions of the Y chromosome (the male chromosome).

The most common genetic cause of declining sperm production is the deletion of a particular part of the Y chromosome. This region, known as the AZF region, is very fragile and susceptible to damage as DNA is assembled and reassembled into genes. Research over recent years has focused on mapping or identifying particular infertility genes in this region and trying to discover ways to stabilize critical DNA areas. If these are identified in advance of assisted treatments, couples can be adequately advised.

Genetic scientists hope to identify specific genes that affect infertility and to possibly correct aberrations with gene therapy techniques. Research in animal models has already demonstrated that defective genes can be removed, reprogrammed, and replaced back into the body to resume normal functions. With this and other new technologies, we can now look optimistically to a brighter future in treating male infertility.

Fast Fact:

Each milliliter of normal semen has at least 50 million sperm, the majority of which are healthy. A low sperm count contains fewer than 20 million sperm.

new fibroids, but none experienced a recurrence of treated tumors.

The use of heat to destroy fibroids is seen as a breakthrough because the procedure may offer women a less-invasive alternative to traditional surgeries and one that does not require staying overnight in the hospital. Some 20 to 25 percent of American women will develop uterine fibroids, a leading cause of hysterectomy. Fibroids also are associated with infertility.

TOSS THIS HERB. If you're pregnant or trying to conceive, you may want to steer clear of ginkgo biloba. The herb, long known for its memory-boosting properties, may contain a toxin that can cause birth defects, according to recent research.

METER YOUR MEAT. Pregnant women should watch the amount of red meat they consume, according to a recent study published in the journal *Hypertension*. The researchers found that those who eat lots of red meat but few carbohydrates may be putting their babies at increased risk of developing hypertension (high blood pressure) later in life. They believe that metabolizing amino acids from a diet rich in protein may place extra stress on the fetus, which can lead to high blood pressure. It's better to eat a balanced diet and to eat no more than three servings of protein daily.

ANOTHER USE FOR ASPIRIN. An aspirin a day may keep preeclampsia away. According to a recent study conducted by researchers at Birmingham Women's Hospital in England, pregnant women who take 60 to 100 milligrams of aspirin daily cut their risk of developing preeclampsia by half. Preeclampsia is a serious condition that causes a pregnant woman's blood pressure to spike and can threaten her life and the life of her child.

The researchers developed their findings after reviewing 39 trials of aspirin intake and women with abnormal blood flow in the uterine artery (those at highest risk of developing preeclampsia). Before taking your daily aspirin, check with your physician.

"Hope is the thing with feathers— That perches in the soul— And sings the tunes without the words— And never stops—at all—" — Emily Dickinson

Ask the Doctors

Q: I am trying to conceive and recently heard that vitamin C may help boost my chances. Is this true?

A: Although it's ideal to eat right years before you get pregnant, it's not too late to take in the necessary nutrients to allow you to conceive. If your body suspects a nutritional deficiency, it may not allow you to get pregnant. Vitamin C, a powerful antioxidant, helps keep your body's mucous membranes lining the entire reproductive tract elastic and resilient. Vitamin C also keeps the cilia (tiny hair-like structures) in your fallopian tubes in good health.

A diet rich in antioxidants, such as vitamin C, has also been found to help protect the heart by preventing blood clots and by improving blood-cholesterol levels. Antioxidants neutralize damaging "free radicals," which oxidize other molecules and cause damage to cells. They also boost immune system function to keep diseases at bay, and research has shown that women in good health have a better chance of conceiving than those in poor health.

Since the body doesn't store vitamin C, you should consume at least 100 mg of vitamin C to maintain optimum health. Good sources of vitamin C are 1 medium guava (165 mg), 1/2 medium papaya (95 mg), 1/2 cup of red bell pepper (95 mg), and 3/4 cup of orange juice (75 mg). Other foods rich in vitamin C are grapefruit, broccoli, sweet potatoes, and dark leafy greens.

Q: I just found out that I am pregnant and am trying to do everything I can to stay healthy. Is it true that some beauty aids I may be using can harm my developing fetus?

A: Yes, they can. In fact the cosmetics industry recently developed a growing family of product lines created for expectant mothers. Skin-care products from Selph, Belly Basics, Mustela, Bella Mama, and Avon's BeComing Mom line feature only ingredients that are safe for use during pregnancy.

Researchers advise not using products with the following ingredients during the first trimester, when most of the baby's important organs are forming:

• **Retin-A and other retinol products.** These Vitamin A derivatives taken topically may have a negative effect because research has shown that taking high doses of vitamin A orally can cause birth defects.

• **Hair dye.** Although the jury's still out on this one, the harsh chemicals in permanent dyes could be absorbed through your scalp. It's better to opt for vegetable dyes, clear glosses, and other gentle color options.

• **Bleaching toothpastes.** If you use one with the active ingredient carbomide peroxide, it could restrict the flow of oxygen to the fetus.

• **Self-tanners.** Since most contain aminopheline, a caffeine derivative, pregnant women should steer clear of these products since no one knows how much caffeine is absorbed into the bloodstream.



NEW TREATMENT FOR FIBROIDS. A

recent study conducted by gynecologists at the Monterey Peninsula Surgery Center found that heat can successfully treat uterine fibroid tumors in women on an outpatient basis. The new procedure, termed radiofrequency ablation, is performed laparoscopically using two small incisions on the abdomen. A needle electrode is then inserted directly into the fibroid, causing it to heat up. When the cells reach a certain high temperature they die, and the regular uterine tissue surrounding it reabsorbs the tumor.

All 79 of the female patients were successfully treated using the new technique and returned to work in an average of three days. After 11 months of follow-up study, most of the women were free of symptoms, including pain and bleeding. Two patients did, however, develop



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Happy Birthday to . . .



Michael Lee Robinson, born on January 21, 2002, to Marcia and Michael Robinson.

Nicholas Edward Webb, born on January 26, 2002, to Christine and Matt Webb. Alexander Jay Falkenstein and Sharon Kay Falkenstein, born on February 14, 2002, to Kim and Joseph Falkenstein. McKenzie Elizabeth Dawson, born on February 17, 2002, to Tracy and Brian Dawson.

Ashley Lauren Clark and Avery Lawrence Clark, born on March 6, 2002, to Sharon and Marc Clark. Catherine Elizabeth Curtis and Justin Henry Curtis born on March 29, 2002, to

Heidi and David Curtis. Katelyn Anne Severns, born on April 10, 2002, to Sharon and Aaron Severns. Andrew Henry Jefferson, born on May 14, 2002, to Mary Lou and Edward

Jefferson. All the babies and parents are doing well. Thank you, DVIF&G!



George S. Taliadouros, M.D., FACOG, the founder and president of the Delaware Valley Institute of Fertility & Genetics (DVIF&G), recently shared his observations and research on male factor infertility with his colleagues at Virtua West Jersey Health System-Voorhees and South Jersey Health Systems. For more on his findings, please read the "The Male Factor," this issue's cover story.