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REPORT

The Intimate Link Between Erectile Dysfunction and Heart Disease

By William Davis, MD



In the early years of my cardiology practice, I was surprised by the number of men with heart disease who also suffered from impotence. In fact, being incapable of having an erection was the norm rather than the exception after heart attack. In those days, impotence was widely attributed to the psychological depression that often followed heart attack.

But closer questioning often revealed a very different story—men would admit that struggles to achieve an erection usually preceded a heart attack or other cardiac event by one, two, or three years. Back then, the pattern of erectile dysfunction and cardiac disease was so widespread, that most in the medical profession attributed it to simple “aging,” as common as wrinkles and constipation.

Today, we know that a convergence of findings relates male impotence—called erectile dysfunction (ED)—with heart disease. The two conditions are varied expressions of a common phenomenon, and are surprisingly similar. If you have one, you’re likely to have the other.

Powerful clinical and scientific experience suggests a close link between erectile dysfunction and heart disease. Studies like the Health Professionals Follow-up Study have revealed the risk factors for erectile dysfunction to be very similar to those for heart disease. Hypertension, smoking, diabetes, high cholesterol, obesity, and physical inactivity all strongly predict sexual dysfunction in men, as they do heart disease.¹

The Massachusetts Male Aging Study of 1,290 men, aged 40–70 years, has documented the extraordinarily high prevalence of erectile dysfunction among aging men: 50% of men at 50 years of age, and 70% by age 70 have erectile dysfunction.² Furthermore, a recent Italian study of men with severe heart disease has uncovered an astounding 93% with erectile dysfunction 24 months before their heart attack or onset of heart disease symptoms.³

As many of us failed to recognize years earlier, these studies reveal that erectile dysfunction and coronary disease are, in many respects, one and the same. The risks are identical, the paths to both are largely the same, though the immediate consequences are different.

ERECTILE PHYSIOLOGY

In their younger years, most men take the physical act of attaining an erection for granted, as natural and automatic as sweating or digestion. But a complex interplay of physiological activities needs to be initiated and precisely coordinated to trigger, achieve, and maintain an erection.

First of all, libido (sexual desire) triggers a sympathetic (adrenaline-dependent) nervous system reaction mediated through the thoracic spinal cord. Also important is tactile stimulation, the pleasurable effect of touch, which is mediated through the acetylcholine-dependent parasympathetic nervous system. Both the sympathetic and parasympathetic forces regulate the release of nitric oxide—the universal artery-relaxing agent—from the cells lining the penile arteries and all its smaller branches. Nitric oxide causes the arteries to enlarge, increasing blood flow into the penile tissues. This is followed by compression of blood-draining penile veins, which causes blood to engorge the penis and create an erection.⁴



A disruption anywhere along the complex chain of events will impair the capacity to have an erection. Any man who has experienced the frustration of male impotence knows that the consequences extend beyond physical dissatisfaction to anxiety, tension, and embarrassment. A common reason for failure of the erectile apparatus is disruption of the path leading to nitric oxide production and blood flow control.

NITRIC OXIDE—A COMMON DENOMINATOR

Nitric oxide is crucial for a normal erection to proceed. A universal substance in biological systems, nitric oxide has a primal, powerful ability to dilate (relax) blood vessels.⁵⁻⁷ In the human body, nitric oxide exerts its dilating effects for only a few moments before being degraded.

In the vessels that supply the heart, healthy arteries enlarge in diameter up to 50% during exercise when sufficient nitric oxide is present. Because of its brief half-life, a continual supply of nitric oxide is required for optimal effect. If the supply of nitric oxide is inadequate, endothelial dysfunction—a core factor in heart disease—is made worse. Endothelial dysfunction can trigger the growth of coronary plaque.⁸

A similar situation develops in the fragile penile circulation. Any disturbance in nitric oxide production lowers the capacity to dilate penile arteries, impairing penile engorgement for erection. Release of nitric oxide is readily sabotaged by many conditions, including elevated levels of cholesterol, high blood pressure, increased triglycerides, smoking, metabolic syndrome and diabetes, and excessive consumption of dietary saturated fat.⁹ If an artery's inner wall can't produce nitric oxide, an abnormal constriction of the arteries to the penis follows, effectively choking off blood flow.

DISRUPTION IN NITRIC OXIDE SYNTHESIS

The body's source for nitric oxide production is the amino acid L-arginine, which is naturally found in many foods. The average American ingests about 3,000–5,000 mg of L-arginine per day, as it is an amino acid naturally contained in many foods. Meats of all varieties, nuts, and dairy products are rich in L-arginine, so the body is accustomed to intake levels of several thousand milligrams every day.



A deficiency of L-arginine, however, does not generally disrupt nitric oxide synthesis because L-arginine availability is not the rate-limiting step in this process. In fact, research over the past five years has identified an endogenous (occurs in the body naturally) inhibitor called “asymmetric dimethylarginine” or ADMA, an amino acid which blocks the production of nitric oxide. By acting as an L-arginine mimic, this damaging look-alike effectively elbows out L-arginine and pushes it off to the side in the biochemical pathway leading to the synthesis of nitric oxide. ADMA is relatively elevated in patients with hypertension, high levels of cholesterol, triglycerides, homocysteine and low-density lipoprotein (LDL), and low levels of high-density lipoprotein (HDL), as well as with aging itself. This inhibitor of nitric oxide synthesis may very well be the common factor shared by all of these abnormal conditions. Increased levels of this detrimental inhibitor (ADMA) block nitric oxide production, leading to endothelial dysfunction.

IMPACT OF METABOLIC SYNDROME

A collection of risk factors that strongly predict heart disease—termed the metabolic syndrome—is also associated with erectile dysfunction. An increasingly prevalent condition, this syndrome includes low HDL, increased triglycerides, high blood sugar, and heightened inflammation and causes a three-fold or greater risk of heart attack, stroke, and diabetes. It is largely attributable to excess weight, poor diet, and inactivity and afflicts at least 47 million Americans, signaling that an epidemic of erectile dysfunction is sure to follow. Indeed, a survey of 2,400 men participating in a health screening revealed that metabolic syndrome increases the likelihood of erectile dysfunction by 48%.¹⁰

Metabolic syndrome is characterized by HDL below 50 mg/dL in women, below 40 mg/dL in men; triglycerides above 150 mg/dL; blood pressure above 130/85 mm Hg; excess abdominal girth, and fasting blood sugar above 100 mg/dL. The likelihood of developing metabolic syndrome escalates sharply above a body mass index (BMI) of 27.

To make matters worse, men with features of the metabolic syndrome are far more likely to have low levels of testosterone, the primary male sex hormone.¹¹ Obesity is also associated with reduced testosterone levels; the greater the excess body weight, the lower the testosterone.¹²

ERECTILE DYSFUNCTION: WHAT YOU NEED TO KNOW

- Men who suffer from erectile dysfunction often have underlying heart disease. The two seemingly different conditions share numerous common risk factors, such as obesity, metabolic syndrome, and low testosterone levels.
- A key pathological process underlying erectile dysfunction and heart disease is endothelial dysfunction, which occurs when arteries are not able to dilate in response to the body's demand for increased blood flow.
- Both erectile dysfunction and heart disease have been linked with impaired activity of nitric oxide, the body's most powerful vasodilator. An endogenous (produced by the body) compound called asymmetric dimethylarginine is an L-arginine analog, which interferes with the production of nitric oxide and may increase the risk for erectile dysfunction and heart disease.
- The amino acid L-arginine provides the body with the starting material to produce nitric oxide.
- Restoring testosterone to youthful levels offers benefits for reducing the risk factors associated with both erectile dysfunction and heart disease, particularly in men with low initial levels of testosterone.
- Dietary supplements such as L-arginine, carnitine, Korean ginseng, DHEA, pomegranate, ginkgo, and flavonoids may offer benefits for erectile function. Carnitine, DHEA, and pomegranate may also be particularly beneficial for a healthy heart.
- If you suffer from erectile dysfunction, be sure to consult your physician to discover the underlying causes and to assess the presence of hidden heart disease.



DECLINING TESTOSTERONE LEVELS

Low testosterone represents another link between erectile dysfunction and heart disease. A man's testosterone levels gradually diminish beginning at age 30. By the time he reaches his 70s, testosterone levels may have dropped to a tenth of youthful levels. Diminishing testosterone levels contribute to loss of muscle, increased body fat, and reduced libido. Fatigue is common, as is depression. Low testosterone levels can also result in reduced concentration, irritability, passivity, loss of interest in activities, and even hypochondria.

Some call the transition period of the mid-40s the "male menopause" or "andropause." The changes are indeed distinct, though not as visible as the female menopause. As there is no external cue comparable to cessation of a woman's menstrual cycle, most men simply dismiss the changes as "getting old."

Testosterone replacement can help to reverse many of the manifestations of reduced testosterone, boosting muscle strength and vigor, restoring lost libido, and helping control weight.¹³

Potential benefits of testosterone replacement in men with low starting levels include:

- Relaxation of vascular tone and partial correction of endothelial dysfunction. This may occur because testosterone increases production of the natural arterial dilator, nitric oxide, and suppresses growth of smooth muscle cells (a constituent of coronary plaques) in arteries.¹⁴
- Improvement in insulin resistance—a critical problem in pre-diabetes and the metabolic syndrome.^{15,16}
- A dramatic reduction in inflammatory proteins such as tumor necrosis factor-alpha and interleukin-1beta.¹⁷

Low testosterone levels have been found to be more common in men with heart disease. In one study, men with confirmed heart disease had lower testosterone levels than healthy control subjects, whereas those with the most severe heart disease had the lowest levels of testosterone.¹⁸



Severe testosterone deficiency, known as "hypogonadism," is present in approximately 2–35% of men with erectile dysfunction.¹⁹ However, lesser degrees of deficiency are common, perhaps present in the majority, depending on the definition of "low" applied, the method of measurement, and the parameter being used to define testosterone (total, free, or bioavailable) deficiency.^{19,20} Most authorities agree that a total testosterone level below 300 ng/dL is clearly low, and that 300–400 ng/dL is low to low-to-normal. Most studies using testosterone replacement for erectile dysfunction have attempted to achieve blood levels of 450–850 ng/dL.

In years past, before nitric oxide and its role in the erectile response was appreciated, testosterone was used to treat sexual dysfunction in men. It proved a partial success as a standalone therapy, resulting in improved erectile potency in 40–60% of men with low-to-normal testosterone levels. The

likelihood of success increased, however, if starting testosterone levels were low (usually defined as below 300 ng/dL), in which case improved erections were experienced by as many as 65% of men, compared with 16.7% receiving placebo; topical testosterone preparations were also noted to be superior to oral replacement or injections.²¹ These findings were confirmed by another study that showed testosterone produced modest improvements in erectile function and libido in men with low-to-normal testosterone levels.²²

Now that we better appreciate the complex sequence of events necessary for erections to occur, it's no surprise that testosterone alone yields less than perfect results. Erectile dysfunction represents more than just low testosterone, which is just one facet of the spectrum of dysfunctional phenomena that cause sexual dysfunction. Nonetheless, when testosterone is combined with popular drugs like Viagra®, success is enhanced to an even greater degree—orgasmic function improves, along with erectile capacity and libido.²⁰ Testosterone also activates penile nitric oxide; ultrasound studies have demonstrated a 27% increase in arterial blood flow into the penis with testosterone supplementation.²³

AN APPROACH TO LOW TESTOSTERONE

Individuals with lower starting levels of testosterone typically need higher doses of testosterone. My clinic advises checking two blood levels before testosterone administration:

1. Total testosterone
2. Free testosterone (The “free” fraction is unbound and represents the active testosterone portion.)

Furthermore, if feelings of sadness, bloating, or weight gain are prominent, it may be beneficial to measure a form of estrogen called estradiol. This form of estrogen can be elevated in men, particularly in those who are overweight, and may trigger these abnormal responses, increasing the risk of heart disease. Estradiol levels above 30 pg/mL are generally considered abnormal. Weight loss can help correct elevated estradiol, as can prescription “aromatase inhibitors,” such as Arimidex®. In addition, a nutritional supplement called chrysin has been shown in the laboratory to inhibit the aromatase enzyme that is responsible for converting testosterone to estradiol.²⁴ You should consult your doctor to determine if this supplement may be helpful for you.

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NATURAL REMEDIES TO ENHANCE ERECTILE FUNCTION

In addition to testosterone, a number of nutritional supplements may either accentuate the effects of testosterone or enhance the artery-dilating effects of nitric oxide.

The path to a healthy erection involves multiple steps, so the “recipe” for success varies among individuals and may involve some trial and error. It’s always worth discussing your erectile function with your doctor, who may need to consider pathological causes of erectile dysfunction. A doctor’s assistance is also necessary if you are considering one of the erection-promoting drugs.



Coming back to the powerful benefits of nitric oxide, one may wonder if it can be taken as a supplement. Unfortunately, the fleeting nature of this molecule makes that impossible. But the body manufactures nitric oxide directly from L-arginine, an amino acid in the diet. The average American generally ingests up to 5.4 grams (5,400 mg) of L-arginine per day through foods, as it is naturally contained in many proteins, especially meat, nuts, and dairy products.²⁹ This amount is generally more than adequate to serve as a substrate for nitric oxide synthesis.

L-arginine also has modest erection-promoting effects in those patients not consuming adequate amounts of L-arginine in the diet. My clinic recommends 3,000–6,000 mg, twice a day, preferably on an empty stomach. Full erection-enhancing benefit may develop slowly and may require up to three months, although some individuals do experience more immediate effects. My clinic has used L-arginine in combination with prescription drugs for erectile dysfunction without complications (e.g. abnormally sustained erections, called “priapism”), but this should be discussed with your doctor. It may be prudent to take a reduced dose of L-arginine when initiating prescription therapy for erectile dysfunction, reserving the full dose of L-arginine only as needed.

Adverse effects of L-arginine are few, such as loose stools at higher doses. Simply cut back on the dose and build up gradually if you experience this. If you have any active gastrointestinal conditions associated with diarrhea or frequent loose stools, such as ulcerative colitis, Crohn’s disease, or malabsorption, first discuss the use of L-arginine with your doctor.³⁰

Another way of increasing nitric oxide in the body is to prevent its rapid degradation by oxygen radicals. Pomegranate and a superoxide dismutase (SOD)-enhancing nutrient called GliSODin® have been shown to favorably affect nitric oxide activity³¹⁻³⁴ and to reverse clinical measurements associated with endothelial dysfunction in humans.^{35,36} In the animal model, pomegranate has been shown to increase penile blood flow and improve erectile response to stimulation.³⁷ In a preliminary study, men with mild-to-moderate erectile dysfunction experienced modest improvements after only four weeks of consuming pomegranate juice each day.³⁸ Pomegranate juice has been reported to mildly inhibit an enzyme pathway that degrades certain medications, though this effect is dramatically less pronounced than that produced by the common beverage grapefruit juice.³⁹

Achieving optimal nitric oxide levels may help:⁴⁰⁻⁴⁴

- Relieve endothelial dysfunction
- Lower blood pressure by promoting vasodilation throughout the body
- Reduce inflammation
- Increase insulin sensitivity.

Carnitine supplements may enhance erections as effectively as testosterone, according to an Italian study. Taking two forms of carnitine, propionyl-L-carnitine, 2,000 mg/day, and acetyl-L-carnitine, 2,000 mg/day, improved erectile function, modestly exceeding the benefit seen with oral testosterone. Interestingly, both testosterone and carnitine also yielded equal improvements in mood and energy.⁴⁵ Another study revealed that propionyl-L-carnitine, 2,000 mg/day, when added to drug treatment with Viagra® increased the likelihood of successful erections in men who were initially unresponsive to the drug alone. Measurably improved erections increased from 23% with Viagra® alone to 68% when the supplement was added.⁴⁶ Carnitine is generally considered safe and well tolerated, mild gastrointestinal symptoms being the only notable side effect.⁴⁷

A deficiency of the adrenal hormone, dehydroepiandrosterone (DHEA) is also believed to play a role in erectile dysfunction. Over a decade ago, the Massachusetts Male Aging Study revealed blood levels of DHEA-sulfate (the major form of DHEA in the blood) to be closely correlated with erectile ability.² Since then, several small trials, including one comparing DHEA, 50 mg/day, with placebo, have uncovered a significantly better erectile response in those taking DHEA.⁴⁸ Individuals with hormone-dependent cancers should consult a physician before taking DHEA.

For centuries, the herb Korean ginseng has been reported to enhance sexual function and desire. Recent studies have confirmed these effects, suggesting that compounds called ginsenosides may produce a nitric oxide-dependent, artery-relaxing effect. A study using Korean ginseng showed an increase in erectile firmness and sexual satisfaction of 60% in men taking ginseng, compared with 30% in those taking placebo.⁴⁹ Another study also showed a 60% response rate in men taking Korean ginseng, 900 mg three times per day, with improvements in penetration and maintenance of erection.⁵⁰ Similar findings were confirmed by a recent Brazilian study, which also revealed that testosterone levels remained unchanged during supplementation, suggesting that erection-enhancing effects may not be mediated by a change in testosterone.⁵¹ Korean ginseng should not be combined with anticoagulant drugs, such as warfarin, or with nonsteroidal anti-inflammatory drugs that can increase bleeding, such as naproxen or indomethacin. Korean ginseng may decrease blood sugar levels, so you should consult a physician before combining the herb with insulin or other antidiabetic medications.⁵²

Ginkgo biloba has displayed variable effects in enhancing erections. In one study of antidepressant-induced sexual dysfunction, 76% of men experienced improved erections and orgasmic function when given 60–240 mg of ginkgo supplement per day. Interestingly, women participants experienced an even greater improvement in sexual function than men.⁵³ Responses can be highly variable, however, with some men experiencing dramatic improvement, while others derive no benefit. Combining ginkgo with aspirin, anticoagulant drugs such as warfarin (Coumadin®), or thrombolytic (clot-dissolving) medications may increase the risk of bleeding. Individuals with a history of hemorrhagic stroke should not use ginkgo prior to discussion with their doctor.⁵⁴

Some interesting possibilities for enhancing erectile function may lie in the world of flavonoids. Flavonoids from red wine (resveratrol and others) and green tea (epigallocatechin and other green tea catechins) are emerging as facilitators of the artery-relaxing effects of nitric oxide.⁵⁵

LIFE EXTENSION'S RECOMMENDED TESTOSTERONE LEVELS

For optimal health—including sexual and cardiovascular function—Life Extension recommends that aging men maintain healthy levels of free testosterone. Life Extension considers optimal levels of free testosterone to be those that are within the upper one-third of the normal reference range for men between the ages of 20 and 29. (Note that the normal reference range varies depending on the laboratory performing the test.)

USING TESTOSTERONE: PRACTICAL CONSIDERATIONS

A prescription is required to obtain testosterone. It can either be formulated by special pharmacies (“compounding pharmacies”), or obtained as a prescription patch, gel, or injection. The prescribed dose depends on the form used and individual response. Some practitioners advise against using oral testosterone, as orally administered hormones must first undergo metabolism by the liver (termed the “first-pass” effect) before becoming available for functions throughout the body.²⁵

Some doctors shy away from prescribing testosterone to enhance mood or energy, preferring to prescribe it only for “hypogonadism,” which is usually defined as a total testosterone level below 200 ng/dL.

My clinic has found testosterone to be useful in men over 40 years old who suffer from erectile dysfunction, have other symptoms such as low energy or mood, and whose total testosterone level is below 400 ng/dL or who have low “free” testosterone (in the lower half of normal laboratory range).

Unfortunately, insurance reimbursement is spotty for testosterone replacement. A doctor may diagnose “hypogonadism” for a starting testosterone level that is below normal, which somewhat increases the likelihood of insurance coverage. Most men, however, do not fall into this flagrantly deficient range; insurers therefore tend to regard testosterone replacement as “cosmetic” and will not provide coverage. Prescription patches generally cost \$3-4 per day. This is one reason our clinic has gravitated towards formulated testosterone creams, as they are far cheaper, usually costing only \$0.50-1.00 per day.

IS TESTOSTERONE SAFE?

Some medical scientists have raised the concern that administration of testosterone may accelerate the growth of hidden prostate cancer; however, the bulk of existing clinical data has not shown an increased risk in prostate cancer with testosterone restoration if levels are low at baseline.²⁶ Data also suggest that testosterone administered to men regarded as having high risk for prostate cancer at baseline does not necessarily increase prostate cancer diagnosis.²⁷

Nonetheless, it is both wise and prudent to have both a prostate exam and a prostate-specific antigen (PSA, a marker for

prostate cancer) blood test before starting testosterone and annually thereafter. It is also a good idea to have a periodic complete blood count (CBC) and liver function testing because of the occasional increase in hematocrit (the proportion of blood occupied by red blood cells) and liver function changes that could potentially develop in some men taking testosterone.²⁸

OPTIMIZING ERECTILE FUNCTION: A RATIONAL APPROACH

Along with a nutritional program to support and optimize erectile health, it is important for your doctor to consider whether any of your current medications are contributing to erectile dysfunction. Common culprits include antidepressants and antihypertensive medications (especially beta blockers like atenolol and metoprolol; angiotensin-converting enzyme inhibitors like lisinopril and ramipril; and calcium channel blockers like diltiazem and amlodipine). Of course, speak to your doctor before stopping any medication.



As heart disease is so closely tied to erectile function, it is also wise to discuss the possibility of hidden heart disease with your doctor if you have erectile dysfunction. Struggles with erectile function usually precede the symptoms of heart disease by several years, so the time to act is now, when your preventive actions are more likely to result in success.⁸ My preferred method to screen for hidden heart disease is a computed tomography (CT) basic heart scan, which yields a heart scan “score.” A CT heart scan should not be confused with a CT coronary angiogram, commonly referred to as a 64-slice CT coronary angiogram. This is performed on the same CT-scanning device, but involves the use of an X-ray dye and far more radiation exposure than the modest amount required for a basic heart scan. A heart scan score greater than zero signifies the presence of coronary plaque—the disease process underlying a heart attack. The higher the score, the greater the plaque formation. In my opinion, a distant second choice is a stress test, though bear in mind this detects only advanced heart disease.

The formula for successful relief of erectile dysfunction will vary from one man to another, but a combination of useful agents, both non-prescription and prescription, can successfully enhance erectile health in the majority. Many of the same agents that support erectile health, including carnitine, pomegranate, and DHEA, may also yield benefits in the cardiac arena.

Dr. William Davis is a practicing cardiologist in Milwaukee, Wisconsin. He is the founder of the Track your Plaque program, a heart disease prevention program that shows how to use CT heart scans to control coronary plaque. He can be contacted through www.TrackYourPlaque.com.

If you have questions about the scientific content of this article, please call one of our Health Advisors at 1-800-226-2370.

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