

HORMONESYNERGY:

ERECTILE DYSFUNCTION

KATHRYN RETZLER ND



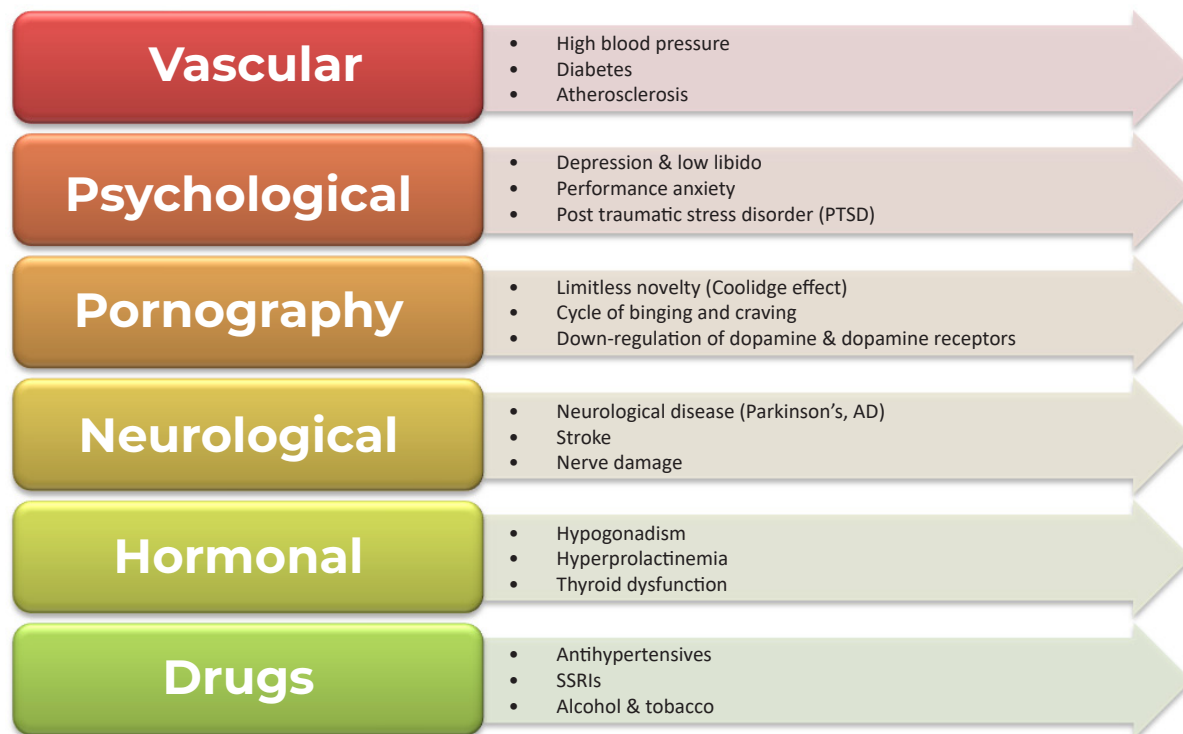
ERECTILE DYSFUNCTION

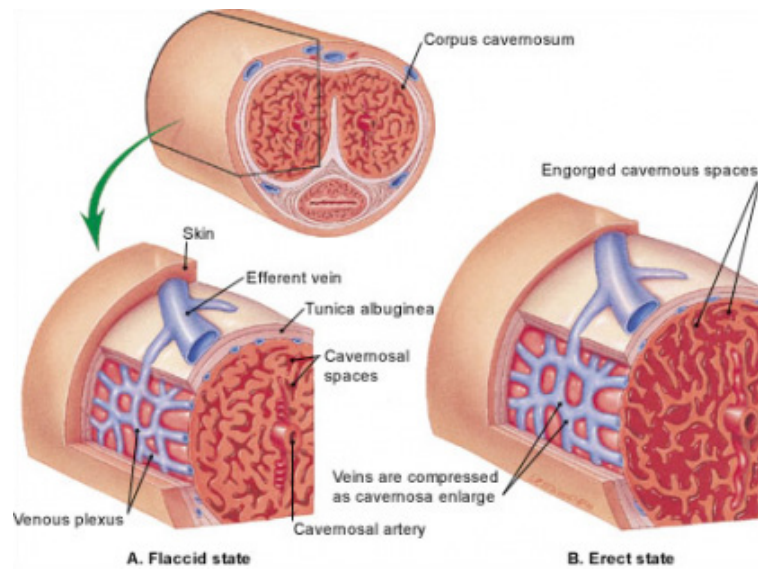
Erectile dysfunction or “ED”—the inability to develop and maintain an erection firm enough for personal satisfaction or penetration—is common with aging. In fact, 40% of men age 40 and 70% of men age 70 have some form of ED. ¹ Unfortunately, even though most men experience transient inability to get or maintain erections, 80% of cases of ED aren’t reported. Hopefully men will feel less embarrassed or uncomfortable discussing sexual issues with their physicians now that celebrities have been featured in ED drug ads, such as Mike Ditka promoting the use of Levitra.

Causes of ED

There are 6 main causes of ED and some men experience more than one cause or contributing factor. These include: blood vessel changes, psychological issues, neurological dysfunction, excessive pornography use, hormonal imbalance, and prescription and non-prescription drugs.

It’s useful to understand all possible causes to develop an effective treatment strategy.





Vascular (blood vessel) changes

Healthy blood vessels are paramount to achieving and maintaining erections. Blood vessel problems are the most common cause of ED in older men—between 70 and 80% of non-psychogenic ED is due to atherosclerosis and vascular dysfunction. Because atherosclerosis in the arteries feeding the heart (“coronary artery disease” or “heart disease”), the brain (“carotid artery disease”) and the legs (“peripheral artery disease”) may only cause symptoms when advanced, ED is often the earliest sign of generalized vascular disease.^{2,3} In fact, ED is as big a risk factor for future cardiovascular events as smoking and family history of heart attacks.⁴ Besides being a predictor of future heart attack, stroke, and heart failure, the presence of ED can predict death from all causes.⁵

ED shares the same risk factors as cardiovascular disease—high blood pressure, lack of exercise, poor diet, smoking, diabetes, and high cholesterol. The underlying mechanism that contributes to vascular-related ED involves endothelial cells that line penile arteries.^{6,7} Endothelial dysfunction increases

ED risk, regardless of clinical evidence of cardiovascular disease.^{8,9} Endothelial cells release a critical chemical called nitric oxide that initiates production of another chemical messenger called cGMP. This causes expansion (vasodilation) of penile blood vessels in the corpus cavernosum, the two columns of spongy tissue that run along the top length of the penis. When the corpus cavernosum fills with blood it stretches, compressing the subtunical venules, the area where blood exits the penis. This compression prevents blood flow out of the penis, producing and maintaining an erection.

Understanding how endothelial dysfunction, insufficient nitric oxide production, and arterial disease cause vasculogenic ED can be helpful in targeting treatments to improve blood vessel health. For detailed information, see Dr. Retzler’s handout “Optimal Cardiovascular Health.”



Psychological causes

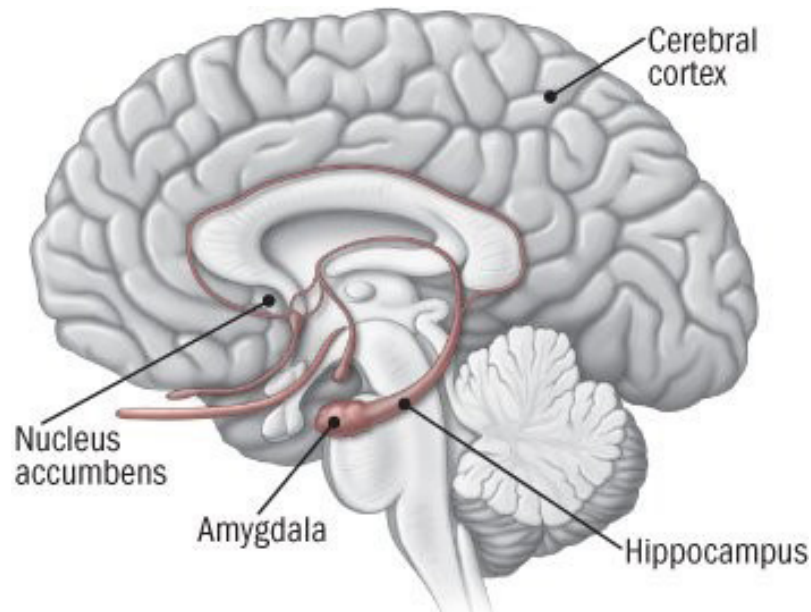
Significant stress, relationship difficulties, depression, anxiety, and post-traumatic stress disorder can all contribute to ED. Anxiety is a normal response to personal and health issues. In addition to life stressors, erectile problems themselves can contribute to anxiety.

Performance anxiety, first described by Masters and Johnson in 1970¹⁰, is an inability to achieve an erection due to past experiences with ED. Men who've experienced severe stress and suffer from post-traumatic stress disorder (PTSD) often have an overactive amygdala (the area of the brain that stores memories associated with fear). 85% of veterans with PTSD report ED vs 22% of veterans without PTSD.¹¹

Depression and stress can certainly contribute to low libido (sex drive) and ED, and ED itself can cause men to feel depressed or struggle with low self-esteem. In fact, ED treatment may actually improve mood in men struggling with depression. In one placebo-controlled trial, 152 men with ED were given Viagra

or a placebo for 6 months; the men who experienced improved erections with Viagra reported less depression and improved quality of life.¹²

If erectile function is normal with masturbation (without using Internet porn), with a different partner, or with different stimuli, psychological causes may be contributing to ED. Nocturnal or morning erections will often be normal and psychologically induced ED may have an abrupt onset or be associated with stress such as job loss, death of a relative, or financial problems. If you think you might have this form of ED, it's best to be evaluated by a psychiatrist, psychologist, or licensed mental health provider.



Neurological problems

The limbic system, including the amygdala, hippocampus, and dentate and cingulate gyrus, is one of the oldest areas of the brain common to all mammals. This brain region regulates emotion and attempts to avoid pain and seek pleasure. Research suggests that sexually-pleasing visual stimuli activate the amygdala and hypothalamus more in men than in women.¹³ Input from the amygdala travels to the ventral striatum, a major portion of the basal ganglia that functions as part of the reward system. The nucleus accumbens within the ventral striatum contains a large concentration of dopaminergic neurons and is considered the brain's pleasure center. Dopamine signaling plays a central role in sexual arousal and motivation. Activation of dopamine receptors in lumbosacral parasympathetic nerves of the spinal cord facilitates erections.¹⁴

Erectile dysfunction from nerve damage is responsible for 10-19% of all causes of ED. Conditions that disrupt normal dopamine signaling or neurotransmission, or that can damage nerves such as Parkinson's disease, multiple sclerosis, diabetes, or stroke, can also cause ED. Surgery, such as removal of the prostate gland due to prostate cancer can cause injury to cavernous nerves for 18 months to 2 years in at least 50% of men^{15 16} however, recovery with time or, possibly, platelet rich plasma (PRP) injections is possible.¹⁷

Long-distance biking can compress the pudendal nerve and blood vessels between the saddle and pubic symphysis, limiting blood flow and oxygen to the penis.^{18 19} Cyclists may experience temporary ED and genital numbness, however they may not have a greater risk for ED. Results of a recent survey of 5,000 athletic men showed that cyclists were just as likely to experience ED as swimmers and runners.²⁰



Pornography Induced ED (PIED)

Although pornography use may be considered socially acceptable and normal, the health risks of frequent use aren't known. To appreciate how pornography can cause ED, it's helpful to understand a phenomenon called the "Coolidge Effect." The term was most likely coined by Frank Beach, a psychologist considered to be the founder of behavioral endocrinology, based on a situation observed between President Coolidge and his wife. The story went like this:

President Coolidge and his wife were individually shown around a farm. When Mrs. Coolidge came to the chicken yard she noticed a rooster who mated frequently and asked how often it happened. When told "dozens of times each day" she said, "Tell that to the President when he comes by." Upon being told, President Coolidge asked, "Same hen every time?" The reply was, "Oh, no, Mr. President, a different hen every time." The President exclaimed, "Tell that to Mrs. Coolidge!"

The Coolidge effect describes a male's renewed sexual interest if introduced to different receptive partners with a possible evolutionary benefit of enabling males to fertilize multiple females.²¹ Novel sexual visual stimuli provoke stronger arousal, firmer erections, and faster ejaculation with more motile sperm and semen production than familiar stimuli.²²⁻²⁴

Internet porn, with its high-speed video and on-demand format, provides limitless novelty (Coolidge effect) and novelty promotes surges of dopamine in the nucleus accumbens, the brain's pleasure center. Dopamine peaks and valleys, changes in dopamine levels, and dopamine receptor abnormalities are involved in many addictions including alcohol, cigarettes, illegal drugs, gambling, and food.²⁵⁻³⁰ The dopamine spike from pornography use is followed by a precipitous drop. Repeated use and over stimulation lead to down-regulation of dopamine and its receptors in the nucleus accumbens, causing desensitization and a numb response to pleasure. Pornography users may then escalate to more extreme material or more frequent use to achieve the same high. Over time, this behavior coupled with down-regulation of dopamine and its receptors rewires connections and pathways in the brain (a phenomenon known as "neuroplasticity")³¹ leading to erosion of willpower, bingeing and craving, and erectile dysfunction (a healthy functioning dopamine system is necessary for normal libido and erectile function).³¹

Pornography use can become an addiction if the user craves it, has lost control over using it, and continues the behavior despite negative consequences. The brain changes that accompany pornography addiction are reversible and breaking the addiction is possible (see treatment section below).

Hormonal

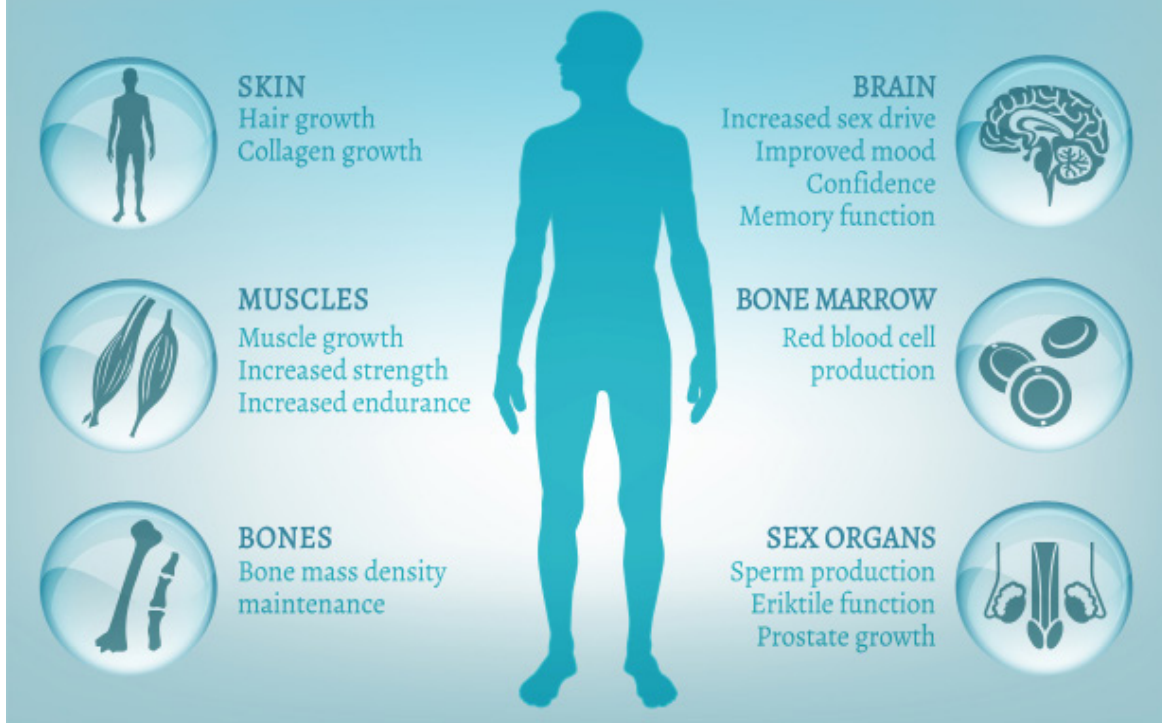
Hormone imbalance may contribute to ED, most commonly reduced testosterone production, low free testosterone, possibly excessive estrogen, elevated prolactin, or thyroid abnormalities.

Besides being necessary for development and growth of the penis and enhancing sex drive, testosterone regulates erectile function via several mechanisms. Testosterone promotes healthy nerve structure, integrity, and function, particularly the cavernous nerve.³³ Animal and human studies suggest that testosterone enhances nitric oxide (NO) production in penile arteries, necessary for vasodilation.³⁴⁻³⁵ Testosterone likely regulates PDE5 activity (the enzyme that is inhibited by drugs like Viagra®) as evidenced by animal studies showing up-regulation of PDE5 expression with testosterone supplementation.³⁶⁻³⁸

Low free and bioavailable testosterone levels, but not total testosterone, are associated with erectile dysfunction. Although the level of testosterone necessary to achieve and maintain erections is unknown, a minimum amount appears to be necessary for erectile function.⁴⁰⁻⁴¹ All men with ED should to be tested for testosterone deficiency.⁴² Testosterone supplementation may not improve all cases of ED; however, some studies have shown that testosterone therapy may be helpful and enable medications such as Viagra and Cialis to work better.⁴³⁻⁴⁴ In addition, libido and sense of well-being can may improve with testosterone supplementation.

Some authors have documented high estradiol levels in men or a high estradiol-to-testosterone

THE EFFECTS OF TESTOSTERONE



ratio associated with ED.^{45 - 47} Medications that inhibit aromatase, the enzyme that converts testosterone into estrogens, may increase total and bioavailable testosterone in elderly men with mild hypogonadism while slightly lowering estradiol levels.⁴⁸ It's important to note that estrogen is healthy for the blood vessels, bone, and the brain. Therefore, lowering estrogen production by treating the cause of increased aromatase activity (obesity, heavy alcohol use, and excess inflammation) is preferable to inhibiting aromatase activity with medications. Currently, there is no evidence that aromatase inhibition improves sexual function and no literature to support the use of aromatase inhibitors for hypogonadism.⁴⁹ In addition, some studies have found the ratio between estradiol and testosterone is unrelated to erectile function or sexual desire.^{50 51}

High prolactin secretion is an uncommon cause of low testosterone and ED. This can be due to a pituitary tumor (prolactinoma) or medications such as amphetamines, H2 blockers, risperidone, SSRIs, MAO inhibitors, and some tricyclic antidepressants. Prolactin should be measured only in cases of low sexual desire, gynecomastia, and/or total testosterone levels less than 4 ng/ml (400 ng/dl).⁵²

An underactive thyroid (hypothyroidism) or overactive thyroid gland (hyperthyroidism) can contribute to ED. In fact, one study of men with thyroid problems found that 79% of the men had ED which was more common with low thyroid function.⁵³ Treatment of hypothyroidism and hyperthyroidism may improve ED,⁵⁴ therefore, screening for thyroid dysfunction in men presenting with ED is recommended.

Prescription Medications & Drugs

Many medications can contribute to ED by affecting neurotransmitters, hormones, nerve function, or blood flow. Although not an exhaustive list, common culprits include antidepressants (especially SSRIs such as fluoxetine, sertraline, citalopram), anti-anxiety medications (benzodiazepines such as clonazepam and alprazolam), sleep aids, antihistamine, CNS depressants and muscle relaxants (lorazepam, cyclobenzaprine). Diuretics (HCTZ, spironolactone, triamterene, furosemide) and antihypertensives and beta-blockers (clonidine, enalapril, metoprolol) also commonly contribute to ED. Studies also link medications for male-pattern hair loss and BPH such as finasteride and dutasteride. ^{55 56}

Consult your prescribing doctor or a pharmacist to see if medications you take may be contributing to ED. Do not stop taking prescription medications without supervision.

Although several types of medications can contribute to ED, one class of over-the-counter and prescription drugs deserve special mention: namely, proton pump inhibitors (PPIs). This class includes Prilosec® (generic is omeprazole), Prevacid,®Protonix,® and Nexium.® These drugs inhibit nitric oxide production which is one of the mechanisms by which they contribute to cardiovascular risk and, possibly, ED. ⁵⁷ Long-term use of PPIs is associated with an increase in heart attack, stroke, cardiovascular death, and kidney disease risk. ^{58 - 61} If you've been taking PPIs for longer than 4 to 8 weeks (the time frame for which these drugs are FDA-approved), your stomach acid may be completely suppressed; abrupt cessation of the drug can cause severe rebound acid secretion. Therefore, tapering the medication over time and replacing it as needed with Rhizinate or GlutamineSynergy (natural products that soothe the stomach lining) or Tums is helpful. Above all, avoid the most common triggers of reflux and heartburn—overeating, eating late at night, coffee and other acidic food such as tomato sauce, spicy food, and alcohol.



Testing for ED



Physicians who've practiced for decades may remember learning about the "postage stamp test" in medical school. This test used a strip of stamps connected by perforations that were secured around a flaccid penis before going to sleep. If the perforated connections were torn upon awakening, nighttime erections were assumed to have occurred.

Thorough evaluation of ED requires a comprehensive history, use of validated questionnaires, physical exam, and lab work. Imaging, such as duplex doppler ultrasound, penile arteriography, and MRI should be performed by a urologist and reserved for potential surgical intervention. If you have risk factors for cardiovascular disease (high blood pressure, elevated blood sugar, cholesterol problems, or family history) or you smoke, or you've had a heart attack or stroke, blood vessel changes are likely contributing to your ED. You should undergo a thorough

cardiovascular work up (including coronary artery CT, carotid IMT measurement, and advanced cardiovascular lab testing).

Genital self-image and sexual frequency expectations are often neglected topics when discussing sexual history, but they significantly affect sexual performance. Results from the development and validation of the Male Genital Self-Image Scale (MGSIS) that assessed men ages 18 to 60 found that men with better genital self-image reported less ED and 20% of men were dissatisfied with their penis size.⁶² Men who have negative genital self-image may wonder how their penis size compares to other men. Alfred Kinsey's data on 2,500 men reported the average flaccid penis length as 1 to 4 inches and an average erect penis as 5 to 6.5 inches. Interestingly, men tended to underestimate their penis size compared to actual measurement.⁶³

Discussing expectations about frequency of sexual activity is relevant for men with low libido, feelings of sexual inadequacy, or curiosity about their sexual frequency compared with other men. Statistics about frequency of sexual encounters is limited. One AARP survey of 1,670 men and women over the age of 45 reported that 41% of men in their 50s, 24% of men in their 60s, and 15% of men in their 70s have sex at least once per week (reframing these statistics—59% of men in their 50s, 76% in their 60s, and 85% of men in their 70s have sex less often than once per week).⁶⁴ The International Society for Sexual Medicine (ISSM), reporting results from the Kinsey Institute's 2010 National Survey of

Sexual Health and Behavior, noted that just under half of married men aged 25 to 49 had sex a few times per month to weekly, which was the highest rate in any age category. ⁶⁵ Another study published by ISSM surveying men and women over age 50 reported that only 20-30% of men and women remain sexually active into their 80s. ⁶⁶

Questionnaires can be very helpful to screen for ED and monitor effectiveness of therapy—the most common are the Sexual Health Inventory (SHIM) test which includes 5 questions and the International Index of Erectile Function (IIEF-5), a 15-question test that’s been validated in 32 languages. The SHIM questionnaire is attached to this handout.

To assess for possible porn-induced ED (PIED) and differentiate it from anxiety-related ED, the following recommendation is from Gary Wilson’s website and book “Your Brain on Porn”:

1. On another occasion masturbate to your favorite porn (or simply recall it).
2. On another masturbate with no porn or porn fantasy (no recalling of porn).
 - Compare the quality of your erection and the time it took to reach orgasm.
 - If you have a strong erection in #1, but ED in #2, you may have porn-induced ED.
 - If #2 is strong, but you have trouble with a real partner, then you have anxiety-induced ED.
 - If you have problems during both 1 and 2, you may have severe porn-induced ED or another problem.

ERECTILE DYSFUNCTION



Treatment of ED

Diet, Exercise, & Fat loss

Stress Reduction & Psychosexual Counselling

Porn-Induced Erectile Dysfunction (PIED)

Physical Therapy

Vacuum Constriction Device (Penis Pump)

Medications: PDE5i, Apomorphine, Intercavernosal Injections

Hormones: Testosterone, Oxytocin

Supplements: Yohimbe, Tribulus, Eurycoma, Nitric Oxide Boosters

Low Intensity Extracorporeal Shockwave (Gainswave)

PRP & Stem cell Injections

Diet, Exercise & Fat Loss



Ideal Body Composition

If you have excess visceral fat or a “spare tire,” commit to a plan to losing it.

Excess and too low of body fat both may increase the likelihood of having ED. For example, the Hallym Aging Study measured body fat percentage and relationship with ED in Korean men.⁶⁷ Men with the lowest and highest body fat were more likely to have ED.

Central obesity (“spare tire”) is associated with low testosterone and blood vessel changes that lead to ED. Fat tissue is not inert—in fact, it secretes more than 35 hormones and cytokines, nearly all of which promote inflammation, insulin resistance, and eventually, vascular disease.^{68,69} Inflammation appears to be a key player in the cause of ED. Obese men with ED have higher levels of inflammatory markers (including IL-6, IL-9, IL-18, and CRP) and impaired endothelial function than obese men without ED.⁷⁰

Weight loss can improve erectile function. In one Italian study, obese men who lost an average of 33 pounds over 2 years regained normal sexual function.⁷¹ The men also reduced oxidative stress and inflammatory markers, improving their overall cardiometabolic risk. More than 30% of men in the weight loss group improved their ED while only 5% of men in the control group reported improvement. The weight loss protocol was simple and easy to implement—men ate 300 fewer calories daily and increased physical activity from 45 minutes to 3 ½ hours per week.



Diet

The search for aphrodisiacs to stimulate libido and improve sexual performance dates to antiquity. Indeed, the word aphrodisiac comes from the Greek Goddess of love, Aphrodite who was born from the sea and brought to shore in a scallop or oyster shell. Although they contain ample amounts of zinc needed for testosterone production, consumption of oysters has not been shown to improve libido or erectile ability. Certain foods, however, do improve vascular health and may, therefore, enhance erectile function.

- **Eat at least 2 cups of green leafy vegetables and/or 1 cup of beet root juice per day.** High blood pressure and ED often coincide due to underlying endothelial dysfunction. Therefore, lowering high blood pressure may also improve ED. In one double-blind study, 34 patients with hypertension given 250 mL (approximately 1 cup) of beet juice daily for 2 weeks reduced their blood pressure.⁷² In another small trial, beet juice lowered blood pressure for 6 hours after drinking a combination of beet and apple juice.⁷³ Beets and green leafy vegetables such as kale, spinach, arugula, and collard greens are especially high in nitrates which get converted to nitrites promoting nitric oxide production to enhance endothelial function.⁷⁴⁻⁷⁶



- **Drink 8 ounces of pomegranate juice or eat pomegranate seeds often.** Pomegranate is full of flavanols, which includes proanthocyanidins—powerful antioxidants that squelch free radicals and protect blood vessels. Eating pomegranate seeds or drinking pomegranate juice can decrease oxidized and glycosylated LDL and remove it from the arterial wall and can reduce carotid IMT (thickness of arterial wall).⁷⁷
⁷⁸ Pomegranate juice also improves nitric oxide production, decreases inflammation, and helps lower blood pressure.^{79 80}



- **Increase your intake of berries either on their own, in smoothies, or as dessert.**

Like pomegranate, berries are high in proanthocyanidins which help strengthen the inner walls and endothelial lining of blood vessels. Randomized, placebo-controlled trials have shown that flavonoids from blueberries improved endothelial and blood vessel function.

⁸¹ Aim for eating at least one-half cup of berries every day.

- **Eat healthy fat. The total amount of fat you eat may not be as important as the type of fat.**

“Healthy fats” include monounsaturated and polyunsaturated fatty acids. Monounsaturated fats are found in olive oil and avocados, as well as nuts such as walnuts, almonds, pistachios, pecans, cashews, and hazelnuts. Good sources of polyunsaturated fats include flaxseed, grapeseed, and fish oils.

“Unhealthy fats” include excessive saturated fat (from animal products), omega-6 fatty acids such as soybean, canola, cottonseed, corn, and vegetable oils, and all trans fats.^{82 83} Trans fats are made by heating liquid vegetable oils in the presence of hydrogen (hence the name, “hydrogenated oil”). It’s relatively easy to avoid eating any trans fats—stay away from commercially packaged baked goods, snack foods, and fast food. Don’t eat any food with “partially hydrogenated oil” on the label, avoid margarine and shortening, and don’t eat fried food in restaurants.

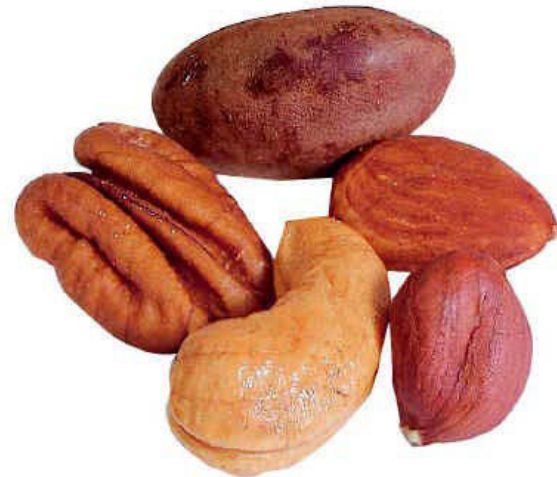


- **Avoid simple or refined carbohydrates such as sugar, soft-drinks, fruit juice, bread, and high-glycemic grains.** This includes crackers, pastries, pretzels, corn chips, bread, pasta, and white rice. These foods dramatically raise blood sugar and stimulate your body to boost insulin, damaging the endothelium and increasing diabetes risk.
- **Avoid soft drinks.** High fructose corn syrup (HFCS) is the main sweetener used in the soft drink industry. It causes greater fat deposition than glucose and negatively impairs



carbohydrate, triglyceride, and lipid metabolism.⁸⁴ Over time, drinking soft drinks and HFCS increases the risk of metabolic syndrome, atherosclerosis, diabetes, and erectile dysfunction.⁸⁵ Excess intake of calories and HCFS leads to the deposition of fat—abdominal or “visceral fat” is a key risk factor for ED.

- **Eat healthy protein.** Protein needs vary based on age, muscle mass, weight goals, and activity level; most men need 0.8 to 1.0 g per kg of body weight (1 lb = 2.2 kg). This translates to approximately 65-90 grams per day (depending on weight and age). Good quality protein includes vegetarian options such as beans and nuts. Animal products such as free-range, organic dairy, eggs, poultry, and lean meat may also be good protein options. Keep in mind that you may need to limit consumption of high saturated fat animal products to improve lipid problems. Wild-caught (not farm raised) fish is an excellent, heart-healthy protein source; to minimize toxin exposure avoid fish high in heavy metals such as tuna and swordfish. Remember the mnemonic SMASH to stick to low mercury fish (salmon, mackerel, anchovies, sardines, and herring).
- **Avoid advanced glycation end products (AGEs).** These compounds are formed inside and outside the body from sugar attaching to proteins or lipids. AGEs damage blood vessels by increasing permeability and stiffness, preventing nitric oxide formation and blood vessel dilation, oxidizing LDL, and promoting free radical activity (oxidative stress) and inflammation. Besides contributing to cardiovascular disease, diabetes, and erectile dysfunction, AGEs literally cause aging.⁸⁶ AGEs form during frying, roasting, and baking (especially any “browning” of food called the “Maillard reaction”).



Different cooking methods substantially affect the AGE content of food; animal-derived foods cooked at high temperatures, especially over prolonged periods of time and under

dry conditions, have the highest AGE content.⁸⁷ Foods that you should avoid due to very high AGE levels include bacon, fast food hamburgers and hot dogs, cheese, pizza, fried food (especially meat, chicken, and potatoes).⁸⁸

- Don't salt your food. Excess salt intake impairs dilation of blood vessels and enhances their constriction, which may reduce penile blood flow.^{89 90} Excess salt also reduces nitric oxide production and endothelial function, independent of changes in blood pressure.⁹¹⁹² Keep salt intake to a maximum of 1500 mg per day. If you ingest more than this, some of the detrimental effects may be ameliorated by potassium, calcium, and magnesium supplementation.

Exercise

Research has shown that exercise is a panacea for addressing conditions that impact erectile function. Medication and supplements cannot achieve the comprehensive health improvements that exercise can—enhancing weight and visceral fat loss, and improving endothelial function, blood pressure, inflammation, and insulin sensitivity.^{93 - 98}

In addition to improving cardiovascular risk and ED, exercise influences the number and function of endothelial progenitor cells (EPCs). EPCs repair blood vessel damage and, unfortunately, decrease with age.^{99 100} A large body of evidence supports aerobic exercise, especially moderate-to-vigorous intensity for a minimum of 8 weeks, in improving erectile dysfunction.¹⁰¹

For exercise to become a way of life, shift your thinking from being a sedentary to an active person. In other words, begin to incorporate changes into your lifestyle such as walking or biking instead of driving and using stairs instead of escalators or elevators when possible.

If you want to get the most benefit from exercise, consider the results of a study comparing moderate continuous exercise and high intensity aerobic interval training.¹⁰² Interval training



was superior in reducing blood sugar and enhancing endothelial function, insulin sensitivity, and muscle mass. Both exercise programs were equally effective at lowering blood pressure and reducing body weight and fat.

Interval training involves a series of high-intensity exercise interspersed with recovery or low-intensity periods. One option is to walk or run at a low-intensity pace for 5 minutes, then increase to high-intensity for 30 to 60 seconds, followed by lower intensity for 60-90 seconds. Repeat this pattern for a total of 8 times (if you're out of shape, start with fewer cycles and work up).

For maximum benefit, you must exercise every 24–48 hours for at least 30–45 minutes at a time. Ideally, combine 20-30 minutes of interval training with strength or weight training. To determine your heart rate zone for intervals, use the updated age-predicted maximum heart rate formula: ¹⁰³

Maximum heart rate = $208 - \text{age} \times 0.7 = \underline{\hspace{2cm}}$

Multiply max HR by 0.70 = $\underline{\hspace{2cm}}$

Multiply by 0.80 = $\underline{\hspace{2cm}}$

Multiply by 0.85 = $\underline{\hspace{2cm}}$

Multiply by 0.95 = $\underline{\hspace{2cm}}$

Heart rate should be 70-80% of maximum during warm up and recovery intervals and 85-95% of maximum during high-intensity intervals.



Stress Reduction

Stress can contribute to psychogenic erectile dysfunction as well as cause blood vessel damage by elevating blood sugar, contributing to insulin resistance, and directly inducing endothelial dysfunction. In fact, psychological stress, in the areas of work, home, finances, and major life events within the past year, has been shown to be a more potent predictor of heart attacks than diabetes, hypertension, and obesity.^{104 105} Brief episodes of stress, such as those encountered in everyday life, cause transient endothelial dysfunction for up to 4 hours.¹⁰⁶ Chronic stress deteriorates endothelial function because hormones and chemicals released under stress, such as glucocorticoids, pro-inflammatory cytokines, and endothelin-1, decrease synthesis and function of nitric oxide.¹⁰⁷

It may be helpful to remember that the feelings and symptoms of stress are due to a sequence of biochemical events in your body. Technically, stress is not an actual event or circumstance—it's your body's reaction to an event or circumstance. This means that stress is not what happens to you—it's how you respond to what happens to you. You can control how you respond to events and circumstances in your life and you can diminish the impact stress has on your body through deep breathing, meditation, and exercise.

Since breathing controls your autonomic nervous system, one simple way to neutralize stress is to focus on your breathing. Transcendental meditation (deep breathing while reciting a specific mantra) has been shown to reduce the incidence of heart disease, heart attack, stroke, and death.¹⁰⁸ Your heartbeat speeds up with every inhalation and slows down with every exhalation. When you feel stressed, focus on lengthening your out-breath. You may want to count—4 counts for each in-breath, 6-8 counts for each out-breath. You will significantly minimize stress and improve parasympathetic activity after only 5 breath cycles.

For more stress reduction tools, please see Dr. Retzler's "Emptying Your Stress Bucket" handout.



Psychosexual Counseling

Individual or couples counseling are helpful in addressing psychological issues underlying ED. If you're struggling with depression and ED, note that the relationship between these conditions is likely bidirectional.¹⁰⁹ In one randomized controlled trial of 152 men with concomitant mild-to-moderate depression and ED, men whose ED improved with sildenafil also had improved mood versus men who didn't respond to sildenafil.¹¹⁰

ED caused by performance anxiety is best treated with individual cognitive behavioral therapy, relationship counseling, or working with a certified sex therapist. There is also evidence that group therapy may improve erectile function. A review of 11 clinical trials, concluded that focused sex-group therapy was more effective than no treatment for ED. A meta-analysis of trials comparing group therapy plus sildenafil citrate versus sildenafil alone, found that men who received group therapy plus sildenafil showed significant improvement of successful intercourse and were less likely than those receiving only sildenafil to drop out. Group therapy also significantly improved ED compared to sildenafil citrate alone.¹¹¹

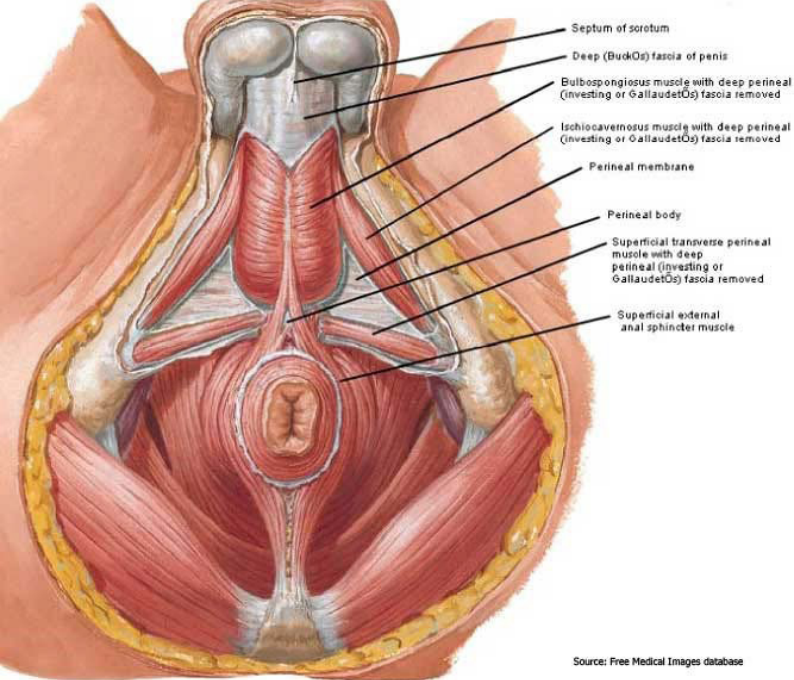
Reconditioning from Excessive Pornography

Use

If excessive pornography use is contributing to ED (porn-induced ED or “PIED”) recovery is possible. Treating PIED requires elimination of porn, porn substitutes, and recalling of porn, i.e., all artificial sexual stimulation. Rewiring healthy sexual arousal requires sexual activity with real people and recovery time is variable. Although the time to “reboot” the brain with pornography avoidance is unknown, pornography addiction expert Gary Wilson suggests clinical experience and online forums show quicker recovery for men over age 50, suggesting that two months is typical.¹¹² Younger men may need more time, possibly up to five months, with the theory that their internet pornography use started at a younger age. Sexual arousal is conditioned, especially during childhood and adolescence, and may be stronger in men than in women.¹¹³⁻¹¹⁵

Withdrawal symptoms from complete porn cessation, such as mood swings, anxiety and panic attacks, agitation, and “flat line”—little or no libido—will fade over time. See the website rebootnation.org for information on porn-addiction recovery and additional resources.





Physical Therapy & Vacuum Constriction Devices

Pelvic floor muscles that play a role in maintenance of erections weaken with age. Physical therapy to strengthen the bulbocavernosus and ishiocavernosus muscles and connective tissue can effectively treat ED. In one randomized, controlled study, 40 men with ED were taught to maximally retract the penis and lift their scrotum twice daily while standing, sitting, and lying down, and to tighten their pelvic floor muscles after urinating. Results were surprising—by six months, 40% of participants regained normal erectile function and 35% showed some improvement; 66% of the men also reported decreased dribbling after urination.

To perform a basic Kegel and strengthen these muscles stop the flow of urine midstream several times during urination. This identifies the muscles that need strengthening. Engage these muscles for 5 seconds, 10-20 times in a row, 3 times per day. Relax and breathe normally and don't clench butt muscles when doing this exercise.

The vacuum constriction device, otherwise known as a "penis pump" was developed by Geddings Osbon in the 1960s who called it a "youth equivalent device." Supposedly, he used the device himself for more than 20 years without it failing while popularizing and perfecting it. The first device to be approved by the FDA in 1982 was called Erecaid®. Vacuum constriction devices are effective for many men due to improving arterial inflow and preventing venous backflow; this increases the volume and rigidity of the penis.¹¹⁶

There are 3 parts to the penis pump: a vacuum cylinder, battery or manually operated pump, and constriction rings. Follow these directions to properly use a penis pump:

1. Place the correct sized constriction ring over the open end of the vacuum cylinder.
2. Apply water-soluble lubricant to the base of the penis to create a tight seal once the vacuum cylinder is placed over it.
3. Generate negative pressure (100–225 mmHg) by hand or battery-operated pump to create an erection.
4. Move constriction ring onto the base of the penis to maintain the erection. Do not leave it on for more than 30 min due risk of ischemia (lack of blood flow).



Medications

Viagra, Levitra, Cialis, & Stendra



The most common medications used to treat ED are in the class called “phosphodiesterase 5 inhibitors” or “PDE5i”. The first drug in this class, Viagra,[®] was introduced in 1998. Since then, 3 other medications have been FDA approved—Levitra,[®] Cialis,[®] and Stendra.[®]

The mechanism of action for all ED drugs is the same—they prolong nitric oxide activity by preventing its breakdown in penile blood vessels. They differ based on selectivity for different PDE isoenzymes (there are 11 isoenzymes identified).¹¹⁷ For example, the PDE6 isoenzyme in the retina transfers light into nerve impulses. Inhibition of this enzyme

causes color perception disturbances called “chromatopsia.” Levitra and Viagra have stronger affinities for this enzyme than Cialis.

No head-to-head trials comparing effectiveness among ED drugs have been performed. These medications differ in onset (time for them to work), duration of action, and side-effects.¹¹⁸ Viagra and Levitra work in approximately 30-60 minutes with a half-life (meaning, half of the drug is metabolized) of 4 hours and duration of activity of 10-12 hours. Cialis has an onset of 1-2 hours, a half-life of 17.5 hours, and duration of 36 hours (lasting the longest). Stendra has an onset of 15-30 minutes (quickest onset) with a 3-hour half-life and 6-hour duration. If these medications are compounded into a troche or lozenge, they may work quicker and the dosage may be reduced (since they can be absorbed in the mouth or under the tongue, bypassing the GI tract).

Side effects of ED meds are common including headache in 10-20% of men, flushing in 5-15%, and nasal congestion (up to 10%). Dizziness, stomach upset, vision abnormalities, and priapism (erection lasting several hours) area is also possible, but much less common. Erections lasting longer than 4 hours are medical emergencies requiring immediate treatment since irreversible damage to the penis may occur.

PDE5i may lower prostate cancer risk, possibly because men who use them may ejaculate more often (high ejaculation frequency is protective for prostate cancer).¹¹⁹⁻¹²¹ Long-term Viagra use is associated with a slightly increased risk for melanoma.¹²²



Apomorphine

Used since 1869 to treat Parkinson's disease, apomorphine is derived from morphine but doesn't contain morphine or bind to opioid receptors and does not cause a person to feel "high." Apomorphine binds to dopamine receptors and may improve libido and erectile function.

In human phase II and III clinical trials involving 5,000 men, 3 to 4 mg of sublingual apomorphine produced erections firm enough for penetration within 10-25 minutes, with approximately 20-25% improvement over placebo.^{123 124} The only patented pharmaceutical apomorphine in the US is injectable Apokyn®, an expensive FDA-approved medication used for advancing Parkinson's disease. Apomorphine can be compounded as a sublingual lozenge and can be combined with a PDE5i. Dosages of 2 to 3 mg may be as effective as 4 to 6 mg without side effects such as nausea, headache, or dizziness.

Intracavernosal Injections

Introduced in 1983, intracavernosal injections modulate endothelial function and are very effective even in men with severe ED. Alprostadil produces erections in up to 93% of men, with effectiveness of bi, tri, and quad-mix of up to 97.6%.¹²⁵⁻¹²⁷ Alprostadil (20 or 40 mcg of prostaglandin E1), marketed as Caverject Impulse® or Edex®, is the only FDA-approved patented intracavernosal injection, whereas

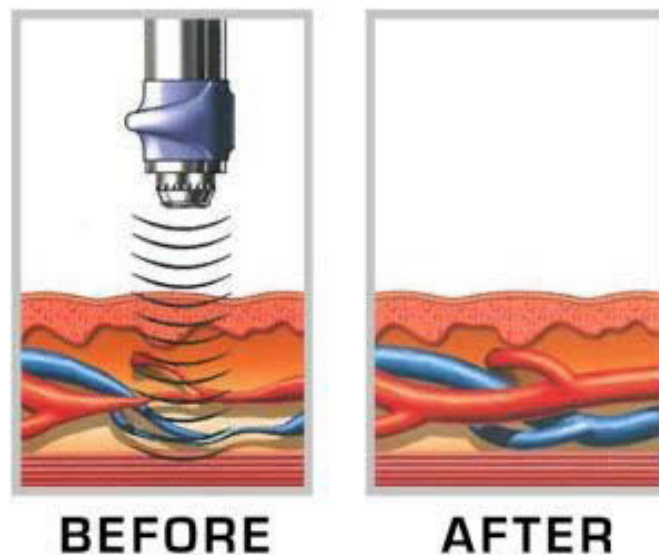


two other medications—phentolamine and papaverine—can be added to PGE1 in a compounded formula. The most common side effect of PGE1 alone is pain in 48.5% of men. Bi-mix, which often contains 0.5 to 3.0 mg of phentolamine and 30 mg papaverine, does not cause pain but may not be as effective. Tri-mix, usually containing 5 to 10 mcg, up to 40 mcg, of PGE1, 0.5 to 1.0 mg phentolamine, and 15 to 30 mg papaverine, reduces pain likelihood to 2.9%. The addition of 0.15 mg of atropine in quad-mix, reserved for men in whom tri-mix is ineffective, significantly ameliorates pain. The amount of PGE1, bi, tri, or quad-mix needed varies from 0.1 to 0.3 ml.

Side effects include pain at injection site, priapism, and development of scar tissue or Peyronie's. For an excellent article reviewing effectiveness, dosages, and side effects of Intracavernosal Injection Algorithm, see Medscape's summary "Intercavernosal Injection Algorithm" by Jeffrey Albaugh.^{128 129}

Gainswave™

Low Intensity Extracorporeal Shockwave Therapy



Low intensity extracorporeal shockwave (LI-ESW) originated in the 1990s using ultrasound to induce blood vessel formation in rat wounds.¹³⁰ Gainswave™ is a procedure that delivers low-intensity extracorporeal shock waves, a type of acoustic shock wave, to improve blood flow to the penis. The mechanism of action for ED improvement appears to be regeneration of penile neuronal nitric oxide (nNOS) positive nerves, improved nitric oxide release, and endothelial and vascular smooth muscle cell repair via recruitment of mesenchymal stem cells.¹³¹ The treatment may also activate local penile progenitor cells.¹³² Currently, LI-ESW is not FDA-approved for ED, however many clinical trials have been performed suggesting it is safe and effective for ED.

The first ED pilot study published in 2010 used six LI-ESW sessions in 20 men who were non-responders to PDE5 inhibitors (PDE5i), meaning that drugs like Viagra® didn't work for them. Results showed improved erectile function, duration of erections, and penile rigidity in one month. Improvements were reported for up to six months of follow up.¹³³

The best studies to determine the effectiveness of any treatment are double-blind, randomized trials (often abbreviated "RCT"). This means that patients are randomly selected to receive treatment or placebo (sham therapy) and neither the patient nor the doctor knows what patients receive. Several randomized, controlled trials have reported positive outcomes using LI-ESW. In one trial involving 67 men with ED who responded to PDE5i, the treatment arm received 12 sessions with improved erectile function in approximately 50% of men without the need of PDE5i.¹³⁴ In a similar RCT in India including 135 PDE5i responders treated with 12 sessions, 78% of

treated men were able to achieve erections firm enough for penetration without medication at one month.¹³⁵ Although these results were sustained at one year follow-up, there was a very high dropout rate including 58% of the sham and 42% of the treatment arms.¹³⁷

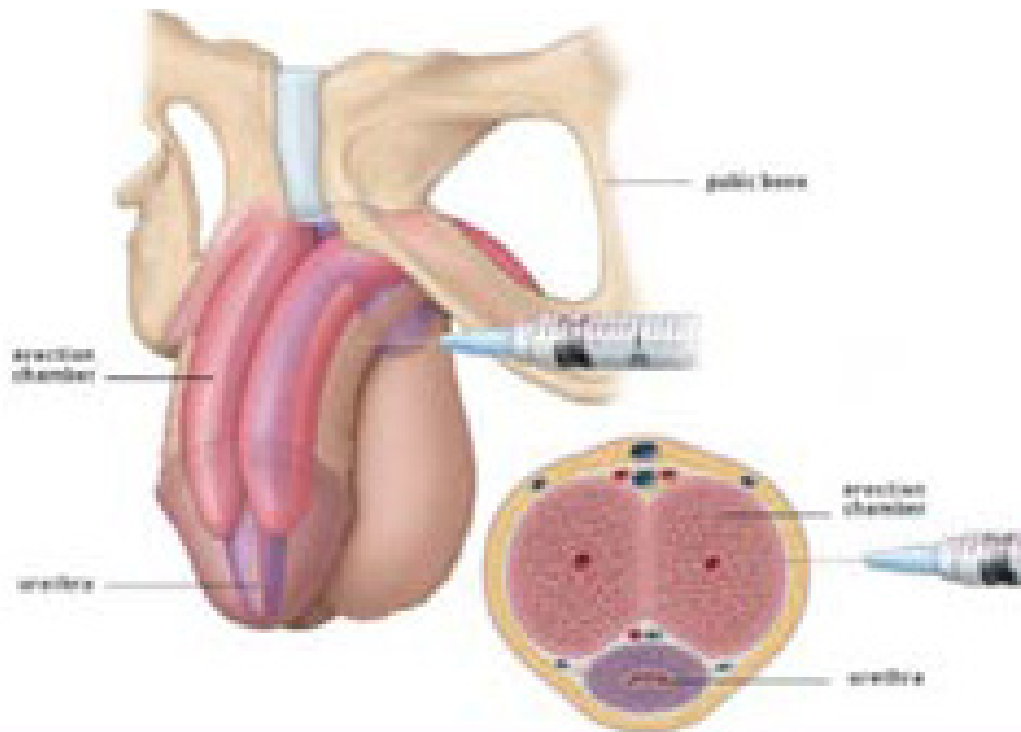
Men who don't respond to PDE5i may become responders after LI-ESW treatment. In an open-label, single-arm prospective study of 29 men non-responsive to PDE5i, 12 treatments resulted in 72% of men able to achieve erections firm enough for penetration with a PDE5i.¹³⁸ In a more recent RCT including 58 PDE5i non-responders, 54% responded to PDE5i after one month of LI-ESW therapy compared to 0% in the sham group.

Sustained improvement seen in longer follow-up studies suggest some men may reverse the underlying problem causing their ED or that LI-ESW may provide some degree of penile rehabilitation. In one RCT with six-month follow-up of 112 men, all of whom received 5 treatment sessions (since the placebo arm received active treatment at 10 weeks), at six months, approximately 20% of the initial treatment arm and 23% of the treated initial placebo group were still able to have intercourse without medication.¹³⁹ Another one-year follow-up of 50 older men (average age 65 years) with vascular risk factors including diabetes, hypertension, dyslipidemia, and coronary artery disease found a 60% sustained improvement in ED severity and self-reported erection quality.

The number of LI-ESW treatments for ideal outcome and how long treatment remains effective are not known. A recent RCT performed on 126 men in a Danish hospital compared men who received ten sessions versus five sessions at 6 and 12 months; treatment was approximately 38% effective in both groups, suggesting that additional sessions may not improve outcome.^{140,141} In a 2-year follow-up of an open-label trial of 156 men, 63% improved at 4 weeks with 53% effectiveness sustained at two years.¹⁴² Not surprisingly, men with severe ED had earlier failure. All patients with diabetes and severe ED lost the effect whereas 76% of men with mild ED and without diabetes preserved effectiveness.

The number of studies using LI-ESWT for ED has increased dramatically in recent years. A narrative review of published literature performed in 2013 reported that 60-75% of PDE5i responders could achieve erections firm enough for penetration without medication and 72% of PDE5i non-responders became responders.¹⁴³ Recent meta-analyses reviewing 14 studies including 7 RCTs found that LI-ESW therapy is safe and effective, with results lasting at least 3 months.^{144,145} Men with mild or moderate ED appear to have a better response than men with severe ED, and energy flux density, number of shock waves delivered, and duration of treatment affect results.

Platelet Rich Plasma (PRP) & Stem Cell Injections



The Priapus Shot or “P-shot” uses platelet rich plasma (PRP) injected into the penis. Platelets in PRP are concentrated from anti-coagulated blood spun in a centrifuge. PRP contains proteins that act as adhesion molecules, and more than 30 bioactive proteins and growth factors, many of which may improve tissue healing and nerve and blood vessel regeneration.¹⁴⁶ Theoretically, PRP may provide benefits in penile tissue similar to improvements seen in orthopedic injuries. Success is likely affected by platelet concentration, volume of PRP delivered, extent of tissue damage or severity of ED, and the overall condition of a patient.

Animal studies have shown improved erectile function and repair of cavernous nerve injury.¹⁴⁷ One small human pilot trial following 17 men with ED or Peyronie’s at an American urology clinic reported improved erectile function and penile curvature with minor adverse effects of mild pain and bruising at the injection site.¹⁴⁸ Another small study at a urology clinic in Italy followed 9 men for one year who were treated with PRP in addition to using a penis pump. Erectile function improved in the men with mild to moderate ED.¹⁴⁹ Regarding Peyronie’s, a small French study involving 13 men with significant penile curvature documented decreased plaque density in 53% with improvement in curvature in 10 men.¹⁵⁰ No human randomized controlled clinical trials have been performed on PRP for ED.

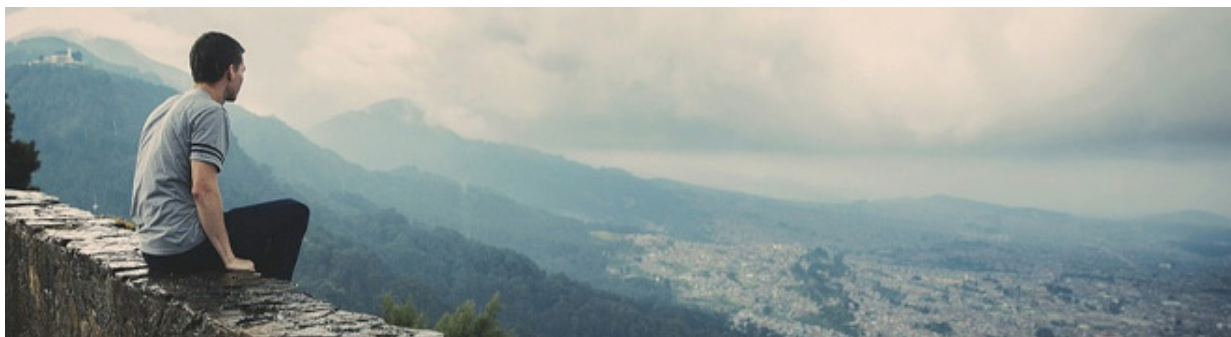
Stem cells are undifferentiated cells capable of becoming different types of cells to regenerate or repair injured tissue. Circulating endothelial progenitor cells (EPCs), critical for blood vessel repair and formation of new blood vessels, are decreased in men with ED and with chronic inflammation, diabetes, hyperlipidemia, obesity, cardiovascular disease, and cigarette smoking.^{151,152} Stem cells injected into cavernous tissue in animal studies have shown promise. In 16 animal studies using stem cells derived from bone marrow, adipose tissue, and skeletal muscle, intracavernosal injection showed favorable outcomes on endothelial, smooth muscle, and nerve improvement in the penis.¹⁵³

Theoretically, PRP and stem cell therapy may be effective in helping men with ED and nerve injuries from diabetes or radical prostatectomy (removal of the prostate which can damage the cavernous nerves). One small pilot study involved 11 men who'd undergone prostate removal due to prostate cancer, with resulting erectile dysfunction that did not respond to PDE5i medications.¹⁵⁴ Adipose-derived stem cells were injected into the corpus cavernosum. 8 of the 11 men (approximately 75%) recovered enough erectile function to accomplish sexual intercourse and no adverse effects were reported. Another small pilot trial involving 7 older Korean men with diabetes and ED that didn't respond to PDE5i medications used umbilical cord stem cell injections.¹⁵⁵ Six men regained morning erections by the third month and two men were able to achieve firm erections with medication with results maintained for 6 months.

Peyronie's

Peyronie's disease (PD) is the development of fibrous scar tissue (plaques) in the tunica albuginea of the penis that causes painful, curved erections. The tunica albuginea is mainly collagen with 5% elastin—this allows the penis to expand and lengthen during an erection. Trauma or micro trauma to the tunica albuginea combined with abnormal wound healing leads to fibrotic nodules/plaque formation.¹⁵⁶ Peyronie's may cause ED due to scar tissue preventing full expansion of corpus cavernosa and compression of veins, allowing venous leakage. Penile curvature may also make penetration difficult. Peyronie's is under-diagnosed with prevalence as high as 9% of men.¹⁵⁷

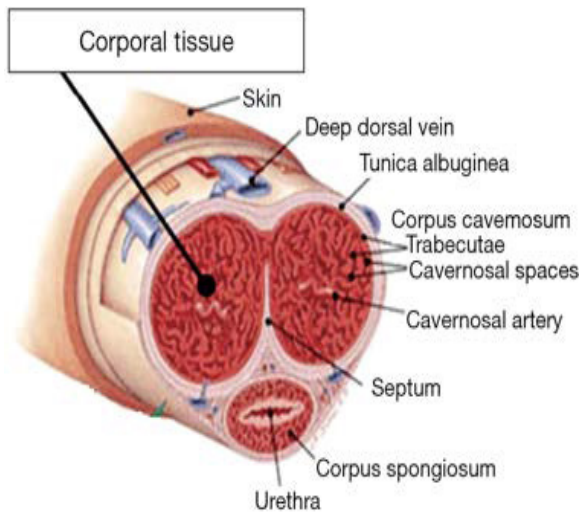
The natural course of Peyronie's over 12 months is complete resolution of pain in nearly all men, with 12% of men improving penile curvature and scar tissue, 40% remaining stable, and



48% worsening.¹⁵⁸ The only FDA-approved, non-surgical treatment for Peyronie's is Xiaflex.[®] In one year, 33-35% of men improve erect penile curvature compared to 18-22% in placebo.¹⁵⁹ If curvature is greater than 60°, severe narrowing ("hinging") occurs, or plaque is large or calcified, surgery may be the only effective option.

Some small studies have shown natural therapies may be effective for Peyronie's. In one RCT, 186 men were given 300 mg of Coenzyme Q10 (CoQ10) or placebo for 6 months.¹⁶⁰ Plaque size and penile curvature decreased overall in the CoQ10 group; 13.6% of men who took CoQ10 experienced disease progression compared to 56.1% of men in the placebo group.

Verapamil, a medication that blocks calcium channels typically used for treatment of high blood pressure, has been used as an injection since 1994. Four studies on verapamil have reported positive results with the mechanism of action assumed to be a decrease in fibroblast proliferation, an increase in collagenase activity, and altering of cytokines.¹⁶¹⁻¹⁶⁶ Younger men with non-calcified plaque and less than 30° curvature may respond better and taking 2,000 mg of L-carnitine, a natural supplement that inhibits free radicals, may improve the result.¹⁶⁷



Other injection therapies—interferon¹⁶⁸, platelet rich plasma (PRP), or autologous stem cells¹⁶⁹—have limited case reports or clinical trials showing effectiveness. Using a vacuum pump (penis pump) may help mechanically straighten abnormal penile curvature. In one study of 31 men who use a penis pump for 10 minutes twice per day for 12 weeks, 21 men had curvature reduction of 5-25°, three men had worsening of curvature, and seven men had no change.¹⁷⁰

LI-ECSW therapy may or may not¹⁷¹ help men with Peyronie's. One small study of 28 men with stable PD who were treated with 3 to 5 sessions of LI-ESWT to the Peyronie's plaque found 71% improvement in erections.¹⁷² Of the 16 men unable to have intercourse before the treatment, 11 were able to afterward due to decreased penile curvature. No complications or side effects were reported.

Another study in 40 men with Peyronie's used only 2 to 3 sessions of LI-ESWT, 2 weeks apart with a maximum of 3000 pulses per plaque treatment.¹⁷³ Average follow up was 1 year. Of the 25 men with painful erections, 48% noticed relief after the first session and 30% were pain-free by the end of treatment. 62% of men showed improved penile angulation.



One RCT including 110 men investigated LI-ESWT alone or combined with low dose Cialis (5 mg daily) in men with Peyronie's.¹⁷⁴ At 3-month follow up, plaque size decreased and quality of life and erectile function improved in both groups, with men using tadalafil in addition to LI-ESWT showing better erectile function. At 6 months, penile curvature degree further decreased and erectile improvements were maintained in both groups.

Meta-analysis of 17 trials using LI-ESWT compared to the natural history of Peyronie's disease suggests that the therapy improves penile pain during erection and sexual function; plaque and lessening of penile curvature improvement appears to be less impressive.¹⁷⁵

Supplements

The use of botanicals, nutrients, and other natural therapies to boost sexual performance has increased considerably due to internet marketing. Few natural therapies have undergone human clinical trials to support safety and efficacy. However, the following botanicals and amino acids may be helpful in treating ED, especially combined with therapies that address the root causes and contributing factors.

Yohimbe

Yohimbe (*Pausinystalia yohimbe*), an evergreen native to central Africa, contains 3 alkaloids in its bark (yohimbine, rauwolscine, and corynanthine) shown to benefit ED.^{176,177} The most active constituent of yohimbe, yohimbine, is a pharmaceutical with a well define mechanism of action as an antagonist of presynaptic $\alpha 1$ and $\alpha 2$ -adrenergic and 5-HT(1B) receptors and partial agonist of 5-HT(1A) receptors.¹⁷⁸

Meta-analyses suggest that yohimbine is effective for ED.^{179,180} Yohimbine may also help with delayed ability or inability to ejaculate.¹⁸¹ Dosage is 15-30 mg, up to 100 mg per day. Yohimbe may be best delivered on-demand since onset is quick, within 10-15 minutes, with a 35-minute half-life. Yohimbine penetrates the central nervous system with possible side effects including



rapid heart rate, hypertension, irritability, and anxiety. Sweating, nausea, dizziness, headache, and skin flushing are also common.

As with all over-the-counter supplements, quality differs between brands. One study testing 49 yohimbe brands found considerable variability in the amount of yohimbine—0 to 12.1 mg—per serving with 19 brands containing no rauwolscine and corynanthine, suggesting they were from highly processed plant extract or synthetic in origin.¹⁸² Companies with good quality yohimbe include Wise Woman Herbals, Herb Pharm, and Gaia Herbs. Side effects include gastrointestinal upset, rapid heart rate, elevated blood pressure, and anxiety.

Tribulus

Tribulus terrestris grows in Europe, Asia, Africa, and the Middle East. The root and fruit have long-term use in both Chinese and Ayurvedic medicine. Animal studies have shown that *Tribulus* improves erectile function and nitric oxide production.^{183,184}

One RCT of 180 men with mild-to-moderate ED using 500 mg of standardized *Tribulus terrestris* taken three times daily reported improved libido, ED, intercourse satisfaction, and orgasm quality.¹⁸⁵ No adverse effects were reported.



Eurycoma or Tongkat Ali

Eurycoma longifolia, known as Malaysian ginseng or Tongkat Ali, is a flowering plant native to Indonesia, Malaysia, Thailand,

Vietnam, Laos, and India. A meta-analysis of randomized controlled trials revealed found that *Eurycoma* significantly improves ED.¹⁸⁶ In addition, a Chinese review of published studies suggest *Eurycoma* improves semen volume, libido, & testosterone.¹⁸⁷ *Eurycoma* may have an adaptogenic



ability, shown to reduce fatigue, improve well-being, lower cortisol, and increase testosterone in stressed subjects.¹⁸⁸ Taken as a water root extract, *Eurycoma* appears safe without significant side effects. Suggested dosage is 200-300 mg once or twice daily, with a patented form standardized to 22% eurypeptides and 40% glycosaponins.

L-tyrosine & L-dopa from *Mucuna pruriens*

Boosting dopamine production in the brain and spinal cord may be helpful for low libido and ED. Exercise, especially learning new skills, improves dopamine production and synaptic connections in the brain.¹⁸⁹⁻¹⁹³ In addition, meditation increases activity of theta waves; increased theta waves correlate with increased dopamine release.¹⁹⁴ Some amino acid precursors may also help support dopamine synthesis. Dopamine is made from L-dopa, which is produced from L-tyrosine with the cofactors iron, BH4, and vitamin B6. *Mucuna pruriens*, known as “velvet bean,” improves sexual behavior in rats and, if standardized for L-dopa level, may improve mood, stress resilience, libido, and sexual performance in men.¹⁹⁵⁻¹⁹⁷

L-arginine, L-citrulline, & Antioxidants

Nitric oxide (NO) is produced by the endothelium (lining) of arteries and is required for arteries to dilate. Optimal NO production by penile arteries is necessary for healthy erectile function. Recall that PDE5i medications like *Viagra*® work by preventing NO breakdown after it’s released. The amino acid L-arginine is the primary substrate for making NO since NO is the byproduct of arginine conversion to citrulline. In addition, L-citrulline supplementation increases plasma arginine and NO synthesis.¹⁹⁸

L-arginine is an amino acid, essential in conditions with increased arginase enzyme such as diabetes and kidney failure.^{199 200} Arginine is used by intestinal and liver cells and converted into L-citrulline or L-ornithine. Variability in absorption of oral L-arginine is considerable with 6 grams being approximately 68% absorbed whereas 10 grams only 20% absorbed. Arginine may improve ED in high dosages; for example, 5,000 mg improves ED, especially if urinary NO metabolites are low.²⁰³ Theoretically, L-arginine may work best if ADMA levels are elevated. Since ADMA inhibits eNOS, the endothelial enzyme needed for NO production, L-arginine supplementation may re-establish the arginine-to-ADMA ratio.²⁰⁴ L-arginine supplementation may be more effective for ED when combined with yohimbine or pycnogenol (pine bark of *Pinus pinaster*).²⁰⁵⁻²⁰⁷ Combining antioxidants such as quercetin and vitamins C & E may preserve NO activity by preventing free radicals from injuring the endothelium. One animal study showed L-arginine, L-citrulline, and vitamins C & E slowed the progression of atherosclerosis in rabbits fed a high-cholesterol diet. L-arginine plus L-citrulline, either alone or in combination with antioxidants, markedly improved



endothelium-dependent relaxation of blood vessels and blood flow. ²⁰⁸ If you take vitamin E, make sure it is not synthetic dL-alpha tocopherol; choose mixed tocopherols (gamma, delta, and d-alpha (the most biologically active)—the forms found in nature).

If you have herpes (cold sores or genital herpes), L-arginine may activate the virus; therefore, don't take L-arginine if herpes outbreaks increase. In addition, high-dose arginine is not safe to use if you've had a recent heart attack. ²⁰⁹

Supplements that may be beneficial:

- **PerforMen's** contains clinically tested LJ100 (standardized extract of Tongkat Ali or Eurycoma longifolia), Tribulis terrestris, and Mucuna pruriens. This synergistic blend supports healthy libido, stamina, vitality, and male sexual performance. LJ100, a proprietary form of Eurycoma, is standardized to 22% eurypeptides and 40% glycol saponins, Tribulis is standardized to 29% saponins, and Mucuna pruriens is standardized to 60% L-dopa to combine the most potent compounds used in clinical studies. Active forms of vitamin B6 and zinc support ideal testosterone and neurotransmitter production. Dosage is 2 capsules, 1 to 2 times per day.



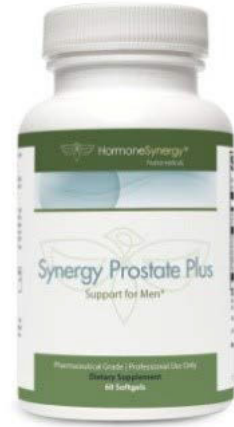
- **Neo40Professional** is a high-potency, quick-dissolve tablet containing concentrated beetroot juice. Neo40 Professional promotes nitric oxide production, enhancing arterial dilation and healthy blood flow.²¹⁰ Using Neo40 twice per day may improve endothelial function and reduce high blood pressure.²¹¹ Supporting healthy endothelial function and blood flow can improve ED. It's important to note that if you are using an acid suppressing medication (such as Prilosec® or omeprazole, Protonix® or pantoprazole, Prevacid®, or Asiphex®), you will likely not respond to Neo40. This is because healthy nitrate-reducing bacteria in the mouth are suppressed with proton pump inhibiting medications. Dosage is 1 tablet dissolved in mouth, twice per day.



- **Test-Protect** is a comprehensive formula designed to support liver detoxification of estrogens and environmental toxins. Milk thistle (standardized to 80% silymarin), alpha-lipoic acid, N-acetyl-L-cysteine, and glucoraphanin as SGS™ and its metabolite sulforaphane are long-acting inducers of antioxidant and detoxification enzymes, including glutathione. Test-Protect also contains diindolmethane (DIM) to promote healthy estrogen metabolism and calcium-d-glucarate to enhance estrogen excretion. Other phytonutrients including green tea catechins, resveratrol and its methylated form pterostilbene, quercetin, and curcumin promote optimal antioxidant activity and reduce inflammation. Dosage is 2 capsules per day.



- **Synergy Prostate Plus** supports normal prostate and urinary tract health and function. SynergyProstate Plus features three well-researched, effective botanicals—saw palmetto (*Serenoa repens*), *Pygeum africanum*, and beta-sitosterol—along with FLOWENS®—a full-spectrum cranberry powder, pyridoxal 5'-phosphate (active B6), and zinc bisglycinate chelate. Saw palmetto has a long history of safely and effectively improving benign prostatic hyperplasia (BPH) symptoms.²¹² *Pygeum africanum* use dates back 300 years and a systematic literature review suggests it also improves urine flow while reducing nighttime urination.²¹³ Lastly, research has shown that that beta-sitosterol significantly improves symptoms of benign prostatic hyperplasia (BPH).²¹⁴ Dosage is 1 to 2 soft gels per day.



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