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# ERECTILE DYSFUNCTION IN YOUNG GENERATION- ETIOLOGY TO POSSIBLE TREATMENT: A COMPREHENSIVE UPDATED REVIEW

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## ABSTRACT
A neurovascular activity involving both spinal & supraspinal channels is an erection. Nitric oxide (NO), a substance that increases blood flow that causes penile engorgement and erection, is released by both endothelial cells and neurons in the final common route. The penis's phosphodiesterase (PDE) type 5 enzyme breaks down NO. The inability to consistently get and/or sustain an erection strong enough for satisfying sexual performance is known as erectile dysfunction (ED). This problem is caused by disruptions in the neurovascular system caused by medicines or medical illnesses. Age-related increases in the incidence of erectile dysfunction (ED) are a consistent finding of epidemiological investigations. However, ED symptoms are growing in frequency, especially among younger men. Medical professionals with expertise in sexual medicine, as well as those working in other therapeutic settings, may be well-equipped to respond to this growing need. Younger men with ED are more likely to have their condition disregarded and ignored without having the most basic medical evaluations, such a physical examination and gathering medical history. This is because it is commonly believed that ED in younger people is a self-limiting illness that can be controlled with patient reassurance alone and does not require clinical assessment or treatment. Fortunately research indicates that biological, psychological, and relational factors may also play a role in the pathophysiology of ED in younger participants. As such, all of these factors may need to be assessed and addressed. Surprisingly, among the organic diseases that contribute to the beginning of ED, risk factors related to metabolism and cardiovascular health (CV) are particularly important in this age range. This review study aims to clarify the origin, pathophysiology, and management of erectile dysfunction.

**KEYWORDS:** Erectile dysfunction, Erection, Cardiovascular, Impotence, Nutraceuticals.

## INTRODUCTION
According to the International Consultation on Sexual Medicine, erectile dysfunction (ED) is the persistent inability to get or maintain an erection strong enough and long enough to have satisfying sex.[1] Up until the 1970s, despite ED's very high frequency, nothing was known about this ailment. Since then, developments in molecular biology methods have significantly enhanced our comprehension of the pathophysiology of ED and penile physiology.[2,3] Integration of the psychological, neurological, and vascular pathways is necessary to get an erection because these routes work together to trigger

a physiological response in the penile vasculature. Nitric oxide (NO) is released by the penile cavernosal tissue in response to parasympathetic transmission from the pelvic splanchnic nerve plexus and the pudendal nerve plexus. Through a cyclic guanosine monophosphate-mediated drop in intracellular calcium, NO causes the cavernosal smooth muscle to relax. By compressing the veins against the tunica albuginea, filling the cavernosal sinusoids prevents blood from leaving the penis, enabling the preservation of an erection.

Phosphodiesterase type 5 (PDE5) is responsible for stopping the brief rise in cyclic guanosine monophosphate. Adrenergic receptor activation causes the cavernosal smooth muscle to contract rhythmically, causing the artery to narrow and causing venous outflow. This process is known as detumescence.[4] The psychological and physiological processes interact in a complicated manner, making it possible for them to get disturbed in a variety of ways and result in ED in young men.

In the past, ED has been thought to be an age-dependent condition, with the majority of men experiencing ED symptoms and indications beyond the age of 65. On the other hand, new research indicates that males under 40 are experiencing an increased prevalence of ED; however, this trend is probably underreported due to younger patients' underreporting.[5] It was thought that ED in males under 40 years old was mostly psychogenic until the 1970s. Consequently, before the 1970s, the only therapies available for young men with ED were behavioral therapies and herbal supplements, together with a nearly complete psychosexual history. Recent studies, which will be outlined further in the following sections of this review, have reported that as many as 87% of young men with ED also have an organic (vascular, neurologic, hormonal, fibroproliferative, or medication-induced) component to their condition.

ED is a serious health issue that has a substantial impact on life enjoyment and can be harmful to a man's psychological health. Since ED is one of the few conditions that would encourage young men to visit a urologist, practitioners need to be more aware of it. Even though endocrine evaluation, oral medication, intracavernosal injection [ICI] therapy, and penile prosthesis are examples of screening and treatment advances that have improved ED detection and management, it is still common for young men with sexual dysfunction to be disregarded without a thorough workup for non-psychogenic etiologies.[6]

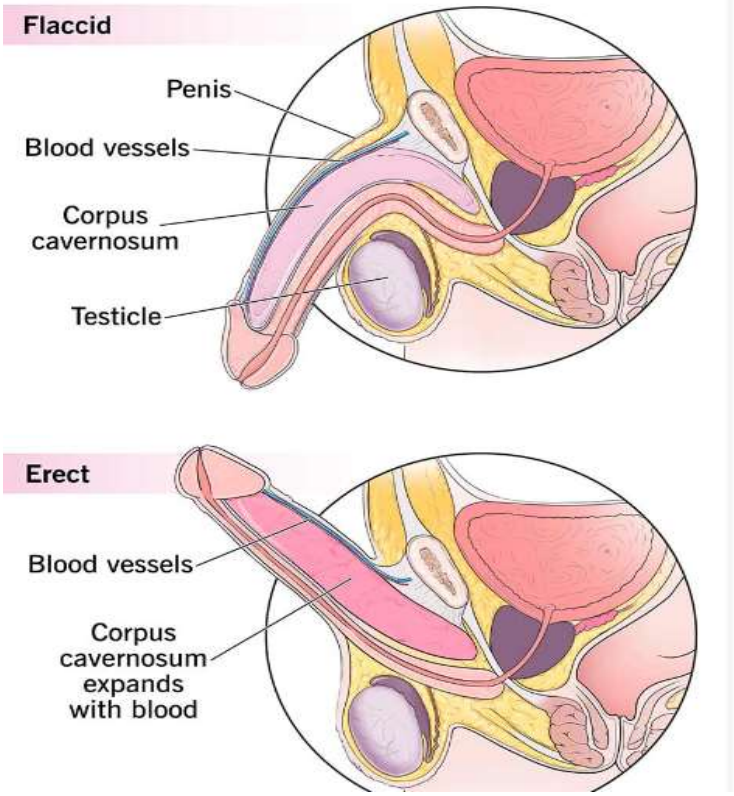


**Figure 1: Top side of figure showing ED pennis, lower showing normal erect pennis.**

**TYPES OF ERECTILE DYSFUNCTION**

Healthcare providers separate ED into several categories: **Vascular erectile dysfunction**. Vascular ED is caused by factors that impact the blood veins in your penis that supply blood to the tissues necessary for achieving and sustaining an erection, as well as the valves that typically keep blood inside the penis. ED that is vascular is the most prevalent kind.

**Neurogenic erectile dysfunction**. Nerve issues that obstruct the transmission of information from the brain to penis to produce an erection are the cause of neurogenic ED. Trauma, pelvic surgery, radiation therapy, or neurological diseases such as multiple sclerosis, spinal stenosis, and stroke can all cause this.

1. **Hormonal erectile dysfunction**. Hormonal ED refers to ED that happens as a result of testosterone deficiency, or in some cases as a result of thyroid issues.
2. **Psychogenic erectile dysfunction**. Psychogenic ED involves psychological conditions (conditions that affect your thoughts, feelings or behavior) that can cause ED.[7]

**ETIOLOGY OF ERECTILE DYSFUNCTION**

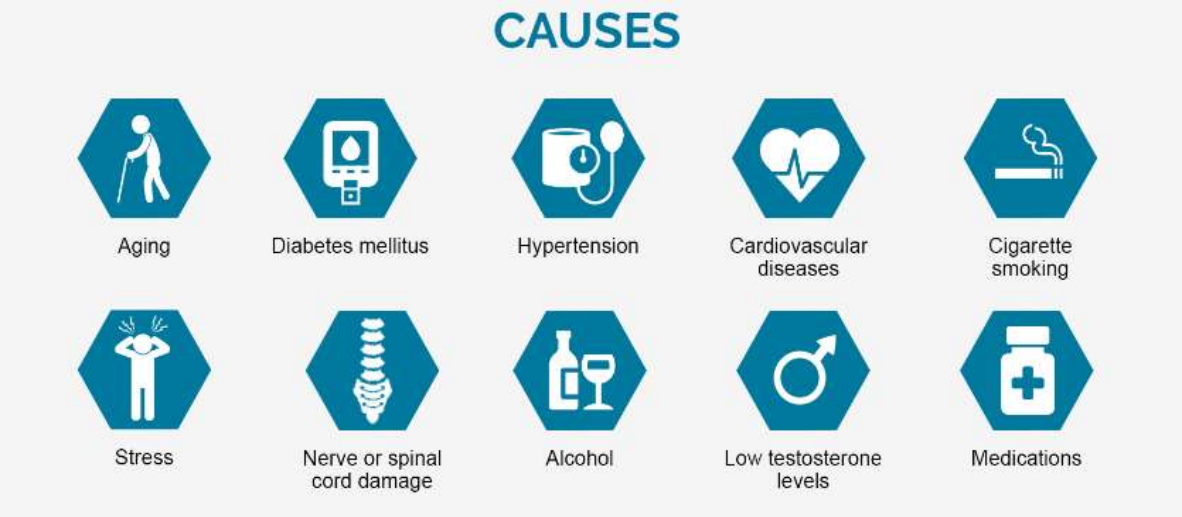


**Figure 2: Possible causes of ED.**

**There are many possible causes of ED**

**1. Inadequate blood flow to Penis**

Blood veins in the circulatory system transport blood throughout the body. Sufficient blood supply to the penis is necessary for erection and maintenance. The penis also depends on a network of valves to shut off as it fills with blood; occasionally, these valves malfunction, leading to problems during an erection.[7,8]

**2. Disturbance in electrical impulses generation**

The nervous system consists of the nerves, brain, and spinal cord. Together, they transmit electrical impulses that support the penis's movement and sensation. Any type of disturbance in the creation of electrical impulses might lead to erectile dysfunction.[7,9]

**3. Testosterone deficiency**

Testosterone may help open up blood vessels, which helps blood flow to your penis. Due to the deficiency of testosterone improper blood flow to penis occurs that results in inadequate erection or erection failure.[7,10]

**4. Diseases and other conditions**

Diseases and other certain conditions may be also responsible for ED. These may include.[7,11,12]

- Diabetes
- High blood pressure
- High cholesterol level
- Vascular disease
- Chronic kidney disease
- Atherosclerosis
- Peyronie's disease
- Stroke.
- Epilepsy
- Penile fracture.
- Injuries to pelvis bones (hip bones, sacrum and tailbone), bladder, prostate and spinal cord.
- Pelvic surgery, including prostate, colon or bladder cancer surgery.
- Radiation therapy

**5. Certain medications**

Erectile dysfunction is a common side effect of many prescription drugs. Common medications that list ED as a potential side effect include:[7,13]

- Antidepressants
- Anti-anxiety medications (anxiolytics)
- Blood pressure medications
- Diuretics
- Antihistamines
- Chemotherapy drugs
- Parkinson's disease drugs
- Prostate cancer drugs
- Antiarrhythmics
- Sedatives
- Muscle relaxers
- Antiseizure medications

**6. Other substances**

Substances that have addiction potential may cause ED, including:[7,14-17]

- Alcohol

- Amphetamines
- Barbiturates
- Cocaine
- Marijuana
- Methadone
- Nicotine
- Opioids

These substances can affect and suppress central nervous system. They can also cause severe damage to blood vessels, which may lead to permanent erectile dysfunction.

**7.** Depression, anxiety, stress, fear of sexual intercourse or intimacy, low self-esteem and other Psychological and/or emotional conditions may also cause ED.[18]

## PATHOPHYSIOLOGY OF ERECTILE DYSFUNCTION

The intracavernosal smoother muscle relaxant is a crucial step in penile erection action. Increased blood flow is made possible by this mechanism, which causes the corpora cavernosa to fill with blood and compress the emissary veins, hence decreasing venous outflow.[19] This mechanism is under the direction of the hypothalamic paraventricular and medial preoptic nuclei. The parasympathetic nervous system sends signals to the parasympathetic nerves in the S2-S4 sacral plexus, which in turn sends signals to the cavernosal nerves, which in turn sends signals to the penis. The erectile process is initiated and maintained by nitric oxide generated by the cavernous nerve terminals and endothelial cells.[8]

When nitric oxide penetrates smooth muscle, it increases the synthesis of cyclic guanosine monophosphate (GMP).Protein kinase G is activated by cyclic GMP, opening potassium channels and closing calcium channels. The intracavernosal smooth muscle tissue relaxes in response to low intracellular calcium, which simultaneously increases veno-occlusive activity and arterial flow.[20] Once the erection is achieved, this leads to a stiff erection with little blood flow into or out of the corpora. The process reverses when the corporal smooth muscle contracts again due to the degradation of cyclic GMP by penile phosphodiesterase. Any of the aforementioned mechanisms might cause pathology that leads to erectile dysfunction.[21]

## FACTORS TO AVOID ERECTILE DYSFUNCTION

### 1. Take a healthy diet

An unhealthy diet for a man's heart is equally detrimental to his erections. Studies have indicated that the same eating habits that might result in heart attacks because of constricted blood flow in the coronary arteries can also prevent blood from flowing to and from the penis.[2] The erection of the penis requires blood flow. Reduced blood circulation throughout the body can result from diets that are high in fat, fried, and processed meals and low in fruits and vegetables. According to Andrew McCullough, MD, head of the male sexual health program at New York University Langone Medical Center and associate professor of clinical urology, everything harmful for a man's heart is equally terrible for his penis. Recent studies show that ED is relatively uncommon among men who eat a traditional Mediterranean diet, which includes fruits, vegetables, whole grains, heart-healthy fats including nuts and olive oil, fish, and wine, particularly red.[22]

### 2. Maintain a healthy weight

Numerous health issues, such as type 2 diabetes, which can harm nerves all over the body, can be brought on by being overweight. ED may occur if the diabetes damages the nerves supplying the penis.[23]

### 2. Avoid high blood pressure and high cholesterol[24]

### 3. Drink alcohol in moderation or not at all.

According to University of California San Francisco School of Medicine urology professor Ira Sharlip, MD, there is no proof that moderate or even modest alcohol intake is harmful to erectile function.[17] Long-term excessive drinking can lead to several health problems, including disruptions in the natural balance of male sex hormone levels, liver damage, nerve damage, and ED. Additionally, excessive drinking may affect one's capacity for erections.[25]

### 4. Exercise regularly

There is strong evidence connecting erectile dysfunction to a sedentary lifestyle. It has been demonstrated that aerobic activity, such as swimming and running, can help prevent ED.[26]

### 5. Avoid anabolic steroids

These substances, which bodybuilders and sportsmen frequently misuse, can induce ED by shrinking the testicles and impairing their production of testosterone.[27]

### 6. Stop smoking

Cigarette smoking can damage blood vessels and reduce the flow of blood to the penis. Additionally, nicotine constricts blood vessels, which can reduce blood flow to the penis and cause ED.[28]

### 7. Curb stress

Stress on a psychological level increases a hormone adrenaline, which causes blood vessels to constrict. That may not be good for getting an erection. Any action a guy takes to reduce stress and improve his mental state will probably have a significant positive impact on his sex life.[29, 30]

## TREATMENT OF ERECTILE DYSFUNCTION

### *1. PDE5-i Treatment*

For erectile dysfunction (ED), oral phosphodiesterase type 5 inhibitors (PDE5i) are the main pharmaceutical intervention. Although sildenafil was initially investigated in clinical studies for the treatment of coronary heart disease, it was sometimes noted that the

medication also improved penile erections. As a result, the FDA authorized sildenafil in 1998 as the first oral medication for ED. There are eleven different PDE isoenzymes in the body, and they are expressed in different tissues at varied concentrations. Although it is present throughout, the PDE5 enzyme is more common in penile tissue. Apart from inhibiting PDE5, sildenafil also exhibits modest suppression of PDE6, an enzyme that is highly prevalent in the retinal rod and cone photoreceptors. This might result in a mild deterioration of color discrimination. This is why the blue pill was designated as the initial PDE5i.[31-33]

### *2. Nutraceuticals*

Numerous randomized controlled trials on the use of dietary supplements or nutraceuticals (ginseng, saffron, Tribulus terrestris, Pinus pinaster, and Lepidium meyenii) in patients with ED were assessed in a recent meta-analysis. L-citrulline and L-arginine have also been suggested as dietary supplements for ED. Though the exact mode of action is yet unknown, each of these seems to boost NO production to some extent. However, before conclusive findings can be made, more extensive and superior research is needed.[34–36]

### *3. Intracavernous Drug Administration*

There are a number of second- and third-line therapy available for people who are not responding to lifestyle changes and medication. The use of intravenous drug administration dates back to the early 1980s; in fact, the pro-erectile activity of papaverine and phentolamine administered within the corpora cavernosa was discovered thanks to the availability of new diagnostic tools like Doppler, which truly revolutionized the way ED patients were treated.[8] Alprostadil (PGE1) was then used in place of these two drugs. It stimulates adenylate cyclase to raise cAMP levels, which results in smooth cell relaxation, vasodilation, and penile erection. Currently, endothelial damage indicated by a decrease in NO availability is treated using pharmacoerection with PGE1. Since the presence of several complications, such as priapism and fibrosis after PGE1 injections, intraurethral devices and cream alprostadil have been proposed as alternative routes of administration.[37]

### *4. Physical Treatments*

Over time, physical therapies for the management of ED have been suggested. The "vacuum device," for instance, is a mechanical device that is cylindrical and is circulated around the penis to suck blood into the area by creating a negative pressure vacuum.38 The adverse effects that were documented were bruises, numbness, and penile discomfort. In addition, low-intensity extracorporeal shockwave therapy (Li-ESWT) has become a popular ED treatment option throughout the last 10 years.[39]

### *5. Surgical Treatment*

Penile revascularization surgery aims to increase penile vascular input while decreasing venous outflow by anastomosing the inferior epigastric artery to the dorsal artery or deep dorsal vein. These methods, meanwhile, were not very successful. Penile prosthesis is actually a desirable and practical surgical strategy for ED patients who are not responding to conventional therapy.[40] Naturally, this method offers a long-term fix for the issue. Inflatable and malleable devices are examples of penile implants. The two semirigid rods that make up the malleable implant are inserted into the corpora cavernosa. However, when an erection is sought, fluid can be delivered to the cylinder chambers of two-piece inflatable penile prosthesis, which consist of two cylinders with a scrotal pump.[41]

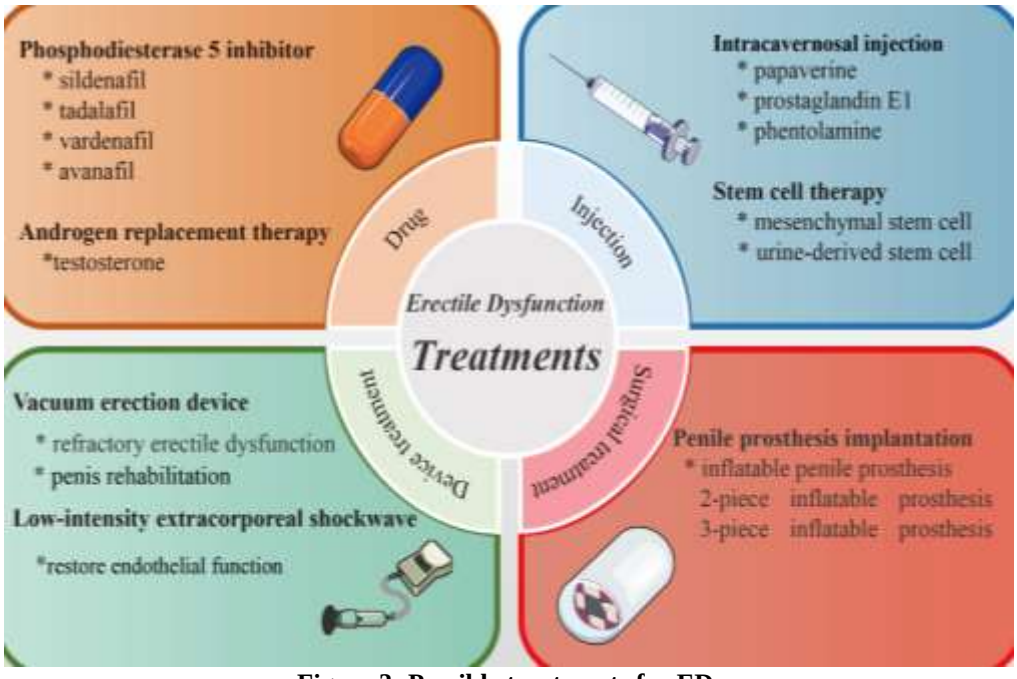


**Figure 3: Possible treatments for ED.**

## COMMON COMPLICATIONS OF ERECTILE DYSFUNCTION

Many problems can arise from erectile dysfunction, both internal and external. It may alter a person's interactions with others, particularly with possible romantic partners. Mental health problems may also result from it. Typical ED side effects include:

- Stress and anxiety about sex
- Low self esteem
- Embarrassment and shame
- Fertility issues
- Relationship problems
- Depression

On the other hand, erectile dysfunction may not always result from mental health problems. It might be challenging to keep an erection going if you suffer from melancholy or performance anxiety related to sex. To address the issue in these situations, the doctor may suggest a combination of therapy and ED remedies.[42–48]

## CONCLUSION

While there aren't many research that explicitly assessed the clinical features of ED in younger men, this issue is becoming more common. Young men who complain of ED are likely to be seen by healthcare experts, both inside and outside of the field of sexual medicine, thus it's critical that there be some fundamental understanding of this subject. In reality, young men who report having ED risk being disregarded without receiving any kind of medical evaluation, such as a physical examination or medical history, because it is believed that ED in its earlier years is a self-limiting illness with no lasting effects. Nonetheless, data indicates that ED may result from a confluence of relational, psychological, and biological variables, just like in middle-aged or older men. Therefore, all of these elements need to be evaluated in order to provide the best possible clinical care. More so than in older men, ED in particular can be regarded as a precursor to CVD and presents a rare chance to identify CV risk factors, enabling high-quality and efficacious preventative therapies.

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