MEDICAL AND SURGICAL THERAPY OF ERECTILE DYSFUNCTION

Shahram S. Gholami, M.D.

And

Tom F. Lue, M.D.

Department of Urology

University of California San Francisco

In this chapter, we will discuss the physiology and pathophysiology of erectile function and dysfunction. We will review the current medical treatments of the disease and the surgical options for patients that fail medical management. Finally, we will mention some of the future treatment options becoming available in the near future.

Erectile dysfunction is defined as the inability to achieve and maintain an erection sufficient to permit satisfactory sexual intercourse.[1] As many as 30 million men in the United States have varying degrees of erectile dysfunction.[2, 3] It may result from impairment of one or more factors: psychological, neurologic, hormonal, arterial, and cavernosal. Epidemiological studies have demonstrated as high as 52% of men in the community have some degree of erectile dysfunction.[3]

Physiology of Erections

Penile erection is a neurovascular event modulated by psychological and hormonal status. Sexual stimulation causes a release of neurotransmitters from the cavernous nerve terminals and relaxing factors from the endothelial cells in the penis resulting in relaxation of smooth muscle in the arteries and arterioles supplying the erectile tissue. A several-fold increase in blood flow occurs with a concomitant increase in compliance of the sinusoids, facilitating rapid filling and expansion of the sinusoidal system against the tunica albuginea. The subtunical venular plexuses are thus compressed between the trabeculae and the tunica albuginea, resulting in almost total occlusion of venous outflow.[4, 5] Blood is trapped within the corpora cavernosa, which causes the flaccid penis to an erect state. Intracavernous pressures are increased to approximately 100 mm Hg (the full erection phase). During sexual activity, the bulbocavernosus reflex is triggered thus causing the ischiocavernosus muscles to forcefully compress the base of the blood-filled corpora

cavernosa and the penis. The penis becomes very rigid, with an intracavernous pressure reaching several hundred mm Hg (the rigid erection phase). During this phase, inflow and outflow temporarily cease.[6] Detumescence can be the result of three separate activities: sympathetic discharge during ejaculation, breakdown of second messengers by phosphodiesterases, or cessation of erectile neurotransmitter release. The venous channels open with contraction of the trabecular smooth muscle therefore expelling the trapped blood and restoring flaccidity.

The penis is innervated by autonomic and somatic nerves. The somatic component is controlled by the pudendal nerve, which is responsible for penile sensation and the contraction and relaxation of the bulbocavernosus and ischiocavernosus striated muscles. The cavernous nerves regulate the blood flow during erection and detumescence. The sympathetic and parasympathetic nerves merge to form the cavernous nerves in the pelvis. The pudendal nerve, the somatic component, is responsible for penile sensation and the contraction and relaxation of the extracorporeal striated muscles (bulbocavernosus and ischiocavernosus).

The principal neurotransmitter for penile erection is nitric oxide, which is released from nonadrenergic-noncholinergic neurotransmission and the endothelium.[7] Nitric oxide activates a soluble guanylyl cyclase raising intracellular concentrations of cyclic guanosine monophosphate (GMP). Cyclic GMP in turn activates a specific protein kinase, which phosphorylates certain proteins and ion channels, resulting in: opening of the potassium channels and hyperpolarization; sequestration of intracellular calcium by the endoplasmic reticulum; and inhibition of calcium channels, blocking calcium influx. The consequence is a drop in cytosolic calcium and smooth muscle relaxation/ erection. During the return to the flaccid state, cyclic GMP is hydrolyzed to

guanosine monophosphate by phosphodiesterase type 5. Other phosphodiesterases are also found in the corpus cavernosum, but they do not appear to play an important role in erections.

Classification of Erectile Dysfunction

Although organic erectile dysfunction is the most common presentation, ED may be classified as psychogenic, organic (neurogenic, hormonal, arterial, cavernosal and drug-induced), and mixed.

Sexual function progressively declines in as men age. The latent period between sexual stimulation and erection increases, erections are less turgid, ejaculation is less forceful, ejaculatory volume decreases, and the refractory period between erections lengthens.[8] There is also a decrease in penile sensitivity to tactile stimulation, decrease in serum testosterone concentration, and an increase in cavernous muscle tone.[9-11]

Erectile dysfunction is noted in patients with neurologic disorders such as Parkinson's and Alzheimer's diseases, stroke, and cerebral trauma. This is caused by a decrease in libido or inability to initiate the erectile process. Spinal cord injury patients have varying degrees of erectile dysfunction largely dependent on the location and extent of the lesion. Sensory input from the genitalia is essential to achieve and maintain reflexogenic erection, and this input becomes more important as the effect of psychologic stimuli abates with age.

About 50 percent of men with chronic diabetes mellitus reportedly have erectile dysfunction. In addition to the disease’s effect on small vessels, it may also affect the cavernous nerve terminals and endothelial cells, resulting in deficiency of neurotransmitters.[7] Chronic renal failure has frequently been associated with diminished erectile function, impaired libido, and

infertility. The mechanism is probably multifactorial: low serum testosterone concentrations, diabetes mellitus, vascular insufficiency, multiple medications, autonomic and somatic neuropathy,[12] and psychological stress. Men with angina, myocardial infarction, or heart failure may have erectile dysfunction from anxiety, depression, or concomitant penile arterial insufficiency.

Psychogenic ED can be caused by performance anxiety, strained relationship, lack of sexual arousability, strained relationship, and overt psychiatric disorders such as depression and schizophrenia. Several studies have confirmed the strong relationship between depression and sexual dysfunction.[13, 14]

Androgen deficiency causing hypogonadism results in a decrease in nocturnal erections and decreases libido. However, erection in response to visual sexual stimulation is preserved in men with hypogonadism, suggesting that androgen is not essential for erection.[15] Due to the inhibitory action of prolactin on central dopaminergic activity and therefore a decrease in gonadotropin-releasing hormone secretion, hyperprolactinemia of any cause results in both reproductive and sexual dysfunction resulting in hypogonadotropic hypogonadism.

Many common medical conditions may induce erectile dysfunction. Common risk factors associated with generalized penile arterial insufficiency include hypertension, hyperlipidemia, cigarette smoking, diabetes mellitus, and pelvic irradiation.[16, 17] Focal stenosis of the common penile artery most often occurs in men who have sustained blunt pelvic or perineal trauma (e.g., biking accidents).[16] Patients with hypertension may develop erectile dysfunction from the associated arterial stenotic lesions associated with elevated blood pressure.[18]

Veno-occlusive dysfunction (VOD) may result from the formation of large venous channels draining the corpora cavernosa. Veno-occlusive dysfunction can cause erectile dysfunction.[19] Venous leak impotence may be the result of degenerative changes that may affect the penis including Peyronie's disease, old age, and diabetes mellitus. A patient may develop VOD from traumatic injury to the tunica albuginea such as a penile fracture. Venous leak can be seen in anxious men with excessive adrenergic tone causing structural alterations of the cavernous smooth muscle and endothelium and insufficient trabecular smooth muscle relaxation.[10] Finally, VOD can be seen in patients with acquired shunts that result from the operative correction of priapism.

Many drugs have been reported to cause erectile dysfunction. Central neurotransmitter pathways, including serotonergic, noradrenergic, and dopaminergic pathways involved in sexual function, may be disturbed by antipsychotics, antidepressants and centrally acting antihypertensive drugs.

Beta-adrenergic blocking drugs may cause erectile dysfunction by potentiating ·-1 adrenergic activity in the penis. Thiazide diuretics have been reported to cause erectile dysfunction by an unknown mechanism. Spironolactone can cause a decrease in libido and gynecomastia as well as causing erectile dysfunction. Cimetidine, a histamine-H2 receptor antagonist, has been reported to decrease libido and cause erectile failure; it acts as an antiandrogen and can cause hyperprolactinemia.[20] Other drugs known to cause erectile dysfunction are estrogens and drugs with antiandrogenic action such as ketoconazole and cyproterone acetate.

Social drugs including cigarettes and alcohol also affect erectile function. Cigarette smoking may induce vasoconstriction and penile venous leakage because of its contractile effect on the cavernous smooth muscle.[21] Alcohol in small amounts improves erections and

increases libido because of its vasodilatory effect and the suppression of anxiety; however, large amounts can cause central sedation, decreased libido and transient erectile dysfunction. Chronic alcoholism may cause hypogonadism and polyneuropathy, which may affect penile nerve function.[22]

Evaluation of Erectile Dysfunction

Erectile dysfunction may be the first manifestation of many diseases including diabetes mellitus, coronary artery disease, hyperlipidemia, hypertension, spinal-cord compression, pituitary tumors, and pelvic malignancies. The evaluation of a patient with ED requires a thorough history (medical, sexual and psycho-social), physical examination and appropriate laboratory tests (UA, CBC, fasting glucose, creatinine, lipid profile, and testosterone) aimed at detecting these diseases. If the man's total testosterone concentration is low, serum free (or bioavailable) testosterone, prolactin, and lutenizing hormone should be further investigated.

After assessing the needs and goals of the patient and his partner, further diagnostic and treatment options should be contemplated. Consideration must be made of the patient's physical and mental health as well as his motivation and needs. The patient's performance status and cardiovascular health also need to be evaluated, if necessary in consultation with a cardiologist, in order to assess the patient's ability to tolerate sexual activity. Occasionally, a change in life-style or medications may be all that is needed to restore potency.

Some men may benefit from a referral for further testing and treatment. The indications for specialty referral include: complex gonadal or other endocrine disorders, neurologic deficit

suggestive of brain or spinal cord disease, deep-seated psychologic or psychiatric problems, Peyronie's disease, post-traumatic or primary erectile dysfunction, and active cardiovascular disease, especially if the patient wishes to take sildenafil.

Medical management of Erectile Dysfunction

Historically, androgens were thought to enhace male sexual function. In this era, androgen therapy should be used in hypogonadal men only. Testosterone therapy in men with normal hormonal levels may increase libido and desire but does not affect ED.[23] Given its many side-effects including hepatotoxicity, skin irritation, dermatitis, stimulation of prostate and cancer growth, testosterone should be avoided in men with normal hormonal levels and men with prostate cancer and BPH. In hypogonadal men suffering from ED, transdermal and intramuscular testosterone therapy are considered more efficacious than oral testosterone preparations.[24, 25] In elderly men, however, androgens do not seem to improve erectile function. Testosterone cypionate and enanthate are often used for replacement therapy; the usual dosage is 200 mg intramuscularly every 2 to 3 weeks. Their major drawback is the severe peaks and troughs of therapy, with high activity in the first week after injection and with a decrease thereafter. Several transdermal testosterone preparations are now available. Daily application of these preparations raises serum testosterone concentrations to within the normal range in over 90 percent of men. The most common adverse effects have been skin irritation and contact dermatitis. These therapies are contraindicated in men with prostate cancer and BPH causing obstructive symptoms due to their ability to stimulate growth of the prostate. Men receiving androgen

replacement therapy require biannual checks with measurement of hematocrit, serum testosterone, lipid profile, and PSA.

Oral therapy with sildenafil (Viagra®), a type 5 phosphodiesterase inhibitor, is considered first line therapy in men with ED.[26] Sexual stimulation releases nitric oxide into the penile smooth muscle. Sildenafil blocks the inactivation of cyclic GMP, which results in increased smooth muscle relaxation and better erections. In the absence of sexual stimulation, sildenafil has no effect on the penis. Numerous placebo controlled studies have been conducted on the safety and efficacy of sildenafil and the results have shown that the number of erections and rates of penile rigidity, orgasmic function, and overall satisfaction were significantly higher with sildenafil than placebo.[27, 28] In terms of safety, over 1600 patient-years of exposure data has been published showing that sildenafil mild to moderate adverse events associated with its usage and these events were self-limited in duration. The most common complaints were headache (16 percent), flushing (10 percent), dyspepsia (7 percent), nasal congestion (4 percent), and visual disturbances/ color sensativity (3 percent). There was difference in terms of adverse or serious cardiovascular events between the sildenafil and the placebo-controlled group.[28] To date, over 10 million prescriptions of sildenafil have been filled in the United States. Since the release of the drug, over 200 deaths temporally associated with sildenafil therapy were reported to the Food and Drug Administration in the U.S. . Sexual activity was thought to be a likely contributor to myocardial infarction, with sildenafil acting as an enable, allowing men not previously active to partake in sexual activity. [29, 30] Therefore, it appears that sildenafil therapy is safe for most men. Men with cardiovascular disease should seek a cardiologist consultation prior to using sildenafil. The combination of nitrates and sildenafil has resulted in

severe hypotension and 16 deaths in the United States. Therefore, nitrate therapy is a contraindication for sildenafil therapy. The American Heart Association has published a guideline for sildenafil therapy.[31] This includes pre-therapy evaluation of cardiac status for men on multiple antihypertensive medications, pre-existing cardiac disease, and men using nitrite medications.[32]

Sildenafil is works best when taken on an empty stomach and reaches maximum plasma concentrations within 30 to 120 minutes (mean 60 minutes). It is eliminated predominantly by hepatic metabolism, and the terminal half-life is about 4 hours. The recommended starting dose is 50 mg taken 1 hour before sexual activity. The maximal recommended frequency is once per day. Two other pharmaceutical companies (Bayer and Lilly) are in the midst of clinical trials to get FDA approval of their phospodiesterase type 5 inhibitors. These newer medications have the added benefit of being a more on-demand type of medication.

Yohimbine is a $\cdot_2$-adrenergic receptor antagonist produced from the bark of the yohim tree. Its effect on erectile function is at best marginal and is therefore not recommended in patients with organic ED. A meta-analysis of several placebo-controlled studies of 419 men with predominantly non-organic ED has shown some benefit over placebo.[33] Frequent side effects include palpitation, fine tremor, elevation of blood pressure, and anxiety.

Oral phentolamine (Vasomax®) has been reported to improve erectile function compared to placebo.[34, 35] Side effects of the medication include headache, facial flushing, and nasal congestion. Oral phentolamine has not been approved by the FDA, but it is available in several South American countries.

Apomorphine, a dopaminergic agonist, is a sublingual medication that is available for use in Europe. Apomorphin is a potent emetic that acts on central dopaminergic (D1/D2) receptors. When injected subcutaneously, it induces erections in rats and humans, but the side effects, notably nausea, seriously limited its clinical usefulness.[36] Sublingual apomorphine has not received FDA approval.

Second line therapy includes vacuum constriction device (VCD), trans-urethral suppositories and intra-cavernous injection (ICI) therapy. VCD is the least expensive. It is cumbersome and gives an unnatural erection. The erection is attained via vacuum suctioning of blood that is trapped in the penis with a constriction device. This type of therapy is preferred for older patients in stable relationships. Its side effects include petechiae, numbness and a trapped ejaculate. Transurethral prostaglandin E1 with alprostadil (MUSE®) has many advantages including local application, minimal systemic effects, and the rarity of drug interaction. However, this type of secondary treatment has failed to gain popularity due to its major drawbacks including moderate to severe penile pain, low response rate and inconsistent efficacy.[37, 38]

Transurethral alprostadil has been extensively studied in Europe and the United States and was found to be effective in 43 percent of men with erectile dysfunction of various organic causes. The most common side effects were penile pain (32 percent) and urethral pain or burning (12 percent).[39, 40] Using an adjustable constriction device (Actis®) placed at the base of the penis after MUSE administration resulted in an increase in success sexual intercourse in 69 percent of men.[41] Patients are initially started with a test dose of 500-µg in the office. Depending on the patient's response, this dose can be titrated from 250-1000 µg. It is

important to administer the test dose in the office due to the risks of urethral bleeding, vasovagal reflex, hypotension, and priapism that can occur with this medication.

There are several available intracavernous medications available including: papaverine, alprostadil, phentolamine, VIP (vasoactive intestinal polypeptide), and ketanserin. Men must receive appropriate training and education by medical personnel before beginning home injections. The goal is to achieve an erection that is adequate for sexual intercourse but does not last for more than one hour. The two major side effects of intracavernous injection are priapism and fibrosis (penile deviation, nodules or plaque). Priapism is preventable through careful titration. To prevent fibrosis, we routinely instruct men to compress the injection site for 5 minutes (up to 10 minutes in men taking anticoagulants). Intracavernous injection therapy is contraindicated in men with sickle-cell anemia, schizophrenia or other severe psychiatric disorder or severe venous leakage.

In the U.S., the most commonly used intracavernous drugs are alprostadil alone or in combination with papaverine and phentolamine (Trimix). Alprostadil's efficacy is superior to papaverine alone and in combination with papaverine and phentolamine it results in erections in more than 70 percent of treated men.[42] The usual dose ranges from 5 to 20 μg. The most frequent side effect is painful erections that occur in 17 to 34 percent of men.[42, 43] This hyperalgesic effect is most prominent in men with partial nerve injury, such as those with diabetic neuropathy and those who have undergone radical pelvic surgery. In addition, alprostadil has a relatively low incidence of priapism (0.35 to 4 percent) and fibrosis (1 to 23 percent).[43-45]

Papaverine is a non-specific phosphodiesterase inhibitor that increases cyclic AMP and cyclic GMP concentrations in penile erectile tissue.[46] Its usual dose ranges from 15 to 60 mg. It is more effective in psychogenic and neurogenic erectile dysfunction (up to 80 per cent) compared to vasculogenic (36-50 per cent). Its advantages include low cost and stability at room temperature. Its major disadvantages are priapism (up to 35 percent), corporal fibrosis (up to 33 percent) and occasional increases in liver function tests.

Phentolamine is a competitive ·-adrenergic receptor antagonist. It must be used in combination with papaverine to produce rigid erections (63-87% success rates).[47, 48] Most urologists use a combination of 30 mg papaverine and 0.5 to 1 mg phentolamine. The side effects of phentolamine include hypotension and reflex tachycardia.

Vasoactive intestinal polypeptide (VIP) is a potent smooth muscle relaxant originally isolated from the small intestine. This medication is only available in Europe. Injection of vasoactive intestinal polypeptid alone does not produce rigid erection,[49] when combined with phentolamine, it produces erections sufficient for sexual intercourse in up to 67 percent of men.[50] Common side effects include transient facial flushing (53 percent), bruising (20 percent), pain at the injection site (11 percent), and truncal flushing (9 percent).

Combinations of medications such as papaverine and alprostadil,[51] ketanserin and alprostadil,[52] and phentolamine and alprostadil[53] have been proven to be superior single medications in efficacy of response. The most effective intracavernous therapy used in the U.S. is a three-drug mixture containing papaverine, phentolamine and alprostadil (Trimix). The usual dose of Trimix solution ranges from 0.1 to 0.5 ml. The response rate to this solution is

reportedly as high as 90 percent.[54] Although widely used in the U.S., it is not approved by the FDA.

Although the response rate to injection therapy is high, in long-term studies 38 to 80 percent of men dropped out.[55, 56] To avoid the cumbersome nature of injection therapy, some men alternate injection therapy with sildenafil or MUSE®, preferring injection in circumstances when an erection of longer duration is desired. Alternatively, in men whom injection therapy alone fails or is insufficient, we recommend the use of injection therapy in combination with a vacuum constriction device.

No transdermal medication has been approved by the FDA for erectile dysfunction and none is available for clinical use. Nitroglycerine cream or paste, alprostadil cream, and a cream containing aminophylline, isosorbide dinitrate, and codergocrine mesylate have been used in pilot studies in men with erectile dysfunction with varing results.[57]

Surgical Management of Erectile Dysfunction

Surgical therapy is an important part of the urologic surgeon's arsenal in the treatment of medically refractory ED. With advances in basic science research, newer pharmacological therapies and potentially future genetic therapy will slowly decrease the indications of surgical therapy. Historically, surgical therapy to treat the flaccid penis did not begin until the turn of the twentieth century. Extraordinarily, similar procedures are still being practiced today. Wooten in 1902 described the ligation of the dorsal vein of the penis as a method for restoring erections.[58] Penile prosthesis surgery was described in the early 1930s.[59] The superficially placed rigid prosthesis made from synthetic material soon followed.[60] It was not until the early seventies

that satisfactory results were seen with the introduction of modern prosthetic devices which fit into the corpora cavernosa and provided both good functional as well as cosmetic results.[59, 61, 62] Penile arterial bypass surgery was first reported in the early seventies as a treatment for erectile dysfunction with many variations in technique existing in the literature. Finally, venous leak surgery was re-introduced in the early eighties to treat corporal veno-occlusive dysfunction. To this day, prosthesis surgery is considered the standard surgical treatment of erectile dysfunction except in a judiciously selected group of patients, which can be offered curative vascular surgical repair.

Young patients with congenital or traumatically acquired ED may be candidates for curative surgical therapy (arterial bypass or venous surgery). Patients with generalized penile disease should be offered prosthesis surgery. Indications for prosthesis surgery include: patients with a poor response to non-surgical therapies; inappropriate candidates for vascular surgery including generalized arterial disease, old age, heavy smokers, drug abusers, and chronic systemic disease. Patients that decline vascular surgery (arterial and venous) or decline to use non-surgical therapies can also be considered for prosthesis surgery after receiving appropriate counseling and detailed informed consent.

Patients considering vascular surgery require a detailed evaluation of the their pelvic and perineal vasculature. Arteriogenic erectile dysfunction is the inability to produce adequate arterial inflow to the cavernosa to achieve an erect state, while venogenic erectile dysfunction is the inability to achieve or maintain erection due to inability to store blood within the corpora cavernosa. Arterial insufficiency can be the result of trauma to the perineum, congenital anomalies (rare),and long-standing systemic disease (hypercholesterolemia, atherosclerosis,

diabeties mellitus). The various causes of veno-occlusive dysfunction have been broadly categorized into the following: ectopic veins, abnormalities of the tunica albuginea (e.g. Peyronie's disease), abnormalities of the cavernosal smooth muscle leading to inadequate relaxation (fibrosis secondary to priapism, aging), inadequate neurotransmitter release, and an abnormal communication between the corpus cavernosum and spongiosum or glans penis secondary to trauma or a surgical shunt procedure to treat priapism.

Arterial Revascularization

Potential curative treatment of erectile dysfunction is available to a select population of patients. Arterial revascularization or venous surgery offers patients the possibility of restoration of normal erectile function without the necessity of medications, injections, or devices. Penile arterial bypass surgery was first described in the early 1970s[63, 64] and has undergone many modifications since its early description. Penile arterial insufficiency is most frequently the result of general arteriosclerosis as seen in other medical conditions with similar risk factors of hypercholesterolemia, hypertension, cigarette smoking, and diabetes mellitus.

Penile arterial insufficiency is diagnosed by performing an intracavernous injection test followed by self stimulation (audiovisual or manual).[65] Duplex ultrasonography of the penis performed during injection and stimulation test can help delineate echogenicity of corporal tissues, peak flow velocity of cavernosal arteries, thickness of tunica albuginea and cavernosal arteries, diameter and wave form of arteries. If duplex ultrasonography after injection therapy is not diagnostic, dynamic infusion cavernosometry/cavernosography (DICC) can be used to further differentiate arterial and venous dysfunction. Finally, once the diagnosis of pure arterial

insufficiency has been confirmed, selective penile/pudendal arteriogram is necessary to identify penile anatomy, demonstrate communication between cavernosal and penile arteries, confirm location of obstructive/traumatized arterial lesion, and plan surgical reconstruction.

Several techniques of revascularization have been desrcribed.[66-69] Current approaches used today either use the technique where the epigatric artery is anastamosed to the dorsal penile artery or the deep dorsal vein. Long term results of these patients has not been outstanding, but with increasing accuracy of diagnostic modalities, improved operative techniques, and a narrowed selection criteria, long term results have significantly improved.[66, 70, 71] Young men with arterial insufficiency secondary to pelvic trauma are the ideal patients for this procedure.[72] Recently, laparoscopy has been used to minimize the morbidity of the procedure.[73] Overall long-term success in appropriately selected patients range from 34-80% spontaneous erections.[66, 74] The most frequent side effects with penile revascularization has been hyperemia of the glans. This can occur in up to 13% of patients. Other complications include infection, hematomas, and thrombosis of vascular anastamosis.

Venous Surgery

Venogenic dysfunction is often suspected during evaluation by the finding of a sub-optimal erectile response to intracavernosal injection despite a normal arterial response on duplex Doppler sonography. The presence of persistent diastolic flow of greater than 5 cm/sec on duplex sonography has also been shown in some studies to correlate with the finding of venous leakage.[75, 76] The gold standard test for the diagnosis of venogenic erectile dysfunction remains the dynamic infusion cavernosometry and cavernosography (DICC). Cavernosometry

and cavernosography can be used to document the severity of venous leakage as well as visualize the sites of leakage.[77-80] An abnormal cavernosometry (after injection of vasodilators to completely relax the penile smooth muscles) is a maintenance rate of greater than 10 ml/min and a drop of intracavernous pressure of more than 50 mm Hg, 30 seconds after the infusion is stopped.[81, 82] An abnormal cavernosogram (performed immediately after cavernosometry) shows visualization of penile veins or venous leakage from the crura on films taken immediately after intracavernous injection of diluted contrast.

Penile venous surgery should be limited to men under age 50 because the high incidence of combined arteriogenic and venogenic impotence in older men leads to an unacceptably high failure rate in this age group. Other relative contraindications to the procedure are: diabetes mellitus, generalized arterial disease, inadequate response to intracavernous pharmacotherapy, and unwillingness or inability to quit smoking. Informed consent should include the risks of possible numbness of the penile skin, shortening of penile length, penile curvature and hematoma. Some investigators also advocate concomitant deep dorsal vein arterialization in order to increase venous resistance.[83, 84]

The lack of long-term success of venous ligation procedures can be partially explained by the complexity of venous drainage of the penis. In the majority of patients, multiple venous leak sites can be visualized on cavernosography. Common leak sites include the superficial and deep dorsal vein, crural veins, corpus spongiosum, and glans penis. The deep dorsal, cavernosal and crural veins are the main venous drainage of the corpora cavernosa and are the most common sites for ligation procedures. Another possible explanation in the widely varied results of venous

surgery in the literature may be due to the many variations of surgical techniques developed to treat patients with veno-occlusive erectile dysfunction.

The reasons for failure of the procedure will vary, but include improper diagnosis, incomplete surgical resection of abnormal venous channels, the presence of an arteriogenic component, and the formation of collateral vessels. In a retrospective review of 50 patients (25 successful and 25 failures) who underwent penile venous surgery the most important factors affecting surgical outcome were the findings on cavernosography and the consequent ease of identification and suture-ligation of the abnormal leak.[85, 86] Those patients with leak into unusual sites, such as the glans, corpus spongiosum, crura in combination with a large amount of drainage to the deep dorsal or cavernous vein had the highest rate of failure. If the venous leak could be easily identified on the cavernosogram and could be suture ligated at the tunica albuginea, success was more likely. Development of venous collaterals and persistent venous leakage appears to be a contributing factor in many patients who fail to improve following venous surgery. Factors that predict a poor prognosis include increasing patient age, duration of impotence, multiple leak sites, proximal (crural) venous leak site, and concomitant arteriogenic insufficiency.[87, 88] At present, in our hands approximately 61% of patients with veno-occlusive dysfunction treated with venous surgery are reported as normal or improved after surgical correction.[89] The etiology of veno-occlusive incompetence remains incompletely understood. As our understand of the cavernosal and sinusoidal function of the penis improves treatment, both medical and surgical, of venous leakage can be directed towards treating the underlying cause rather than a symptom of the disease.

Prosthesis Surgery

There are two general types of prosthesis: semi-rigid and inflatable. The semi-rigids are further divided into malleable and mechanical devices. The malleable prostheses made of silicone rubber with a central intertwined metallic core. Mechanical devices are also made of silicone rubber with interlocking rings in a column, which provide rigidity when the rings are lined up in a straight line and flaccidity when the penis is bent. The advantages of semi-rigid devices are that they are easy to implant, have few mechanical parts with minimal mechanical failure, and generally last longer than inflatable devices. The major disadvantage of the semi-rigid devices is that the penis is neither fully rigid nor fully flaccid. These devices are difficult to conceal with a higher likelihood of device erosion.

There are three types of inflatable prostheses, the one-piece, two-piece, and the three-piece prostheses. The one-piece device consists of a pair of hydraulic cylinders implanted within the corpora cavernosa. A pump at the distal end cycles fluid from a rear tip reservoir into a central chamber to produce penile rigidity. When inflated these devices did not provide expansion, but were equivalent to the semi-rigid prosthesis with respect to their rigidity. Once deflated, the provided a more natural appearing erection than the malleable predecessors. These devices did not meet overall expectations and are rarely used in the United States. Two-piece inflatable prostheses consist of a pair of cylinders attached to a scrotal pump/reservoir. The prosthesis can be deflated by bending the penis at midshaft. These two-piece prostheses also have not been that successful. When fully erect, they are not as rigid as the three-piece device and do not provide the girth expansion. In the flaccid state, they are not as flaccid as the three-piece prosthesis and yet bare a similar risk to infection as a multiple component device. Finally, three-piece inflatable prostheses consist of a pair of penile cylinders, a scrotal pump, and a

supra-pubic reservoir. They provide better rigidity when erect and a more natural appearance when flaccid.

Hydraulic, three-piece implants have been the most popular, accounting for 85% of the market, and give the most natural function. About 15% of patients choose semi-rigid rod implants, and those with limited mental or manual dexterity are encouraged to have this type of device. In general, the semi-rigid devices last longer than the inflatable prostheses. Most devices will need to be replaced by 10-15 years. Repair rates of 5%-20% in the first five years are realistic. Problems with device erosion and infection still occur, although they are less catastrophic. Techniques to correct these with corporoplasty and salvage have proven successful in the majority of these cases.

Satisfaction of the patient and partner with implants has been very good, in the range of 80% or higher. A smaller penile size, lack of spontaneity, and unmet expectations regarding sensitivity, arousal and enjoyment are reasons for disappointment with results. Since non-surgical treatments have a high success rate in improving ED, a penile implant should be reserved only for patient who failed or dissatisfied with non-surgical therapy. Prior to surgery, it is important to review the risks and complications associated with prosthesis surgery. The patients should be shown a representative prosthesis and receive instruction on how it works. The risks of infection, malfunction, and erosion should be explicitly stated to the patient and he should be aware that if complications occur, the prosthesis may need to be removed, replaced or repaired.

Conclusions

As our understanding of the basic mechanisms of erectile function continues to grow, new therapies will emerge in the treatment of erectile dysfunction with the eventual goal of eliminating the need for surgical treatment of the disease. We have witnessed a dramatic change in the treatment of men with erectile dysfunction. Treatment options have progressed from psychosexual therapy and penile prostheses in the seventies, through arterial revascularization, vacuum constriction devices, and intracavernous injection therapy in the eighties, to transurethral and oral drug therapy in the nineties and perhaps gene therapy in the new millennium. Gene therapy may begin to define a place in the urologist's armamentarium, in order to help restore corporal, neural, vascular and tunical tissues in the penis to their normal state.

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LEGENDS

Figure 1

Penile venous surgery demonstrating bilateral proximal crural ligation with resection of the deep dorsal vein.

Fig. 1. Anatomy and Mechanism of Penile Erection. The cavernous nerves (autonomic), which travel posterolaterally to the prostate, enter the corpora cavernosa and corpus spongiosum to regulate penile blood flow during erection and detumescence. The dorsal nerves (somatic), a branch of the pudendal nerve, are primarily responsible for penile sensation. The neurotransmitters for and the mechanism of flaccidity and erection are shown in the upper and lower insert respectively. In the flaccid state, inflow through the constricted and tortuous helicine arteries is minimal, and there is free outflow via the subtunical venular plexus. During erection, relaxation

of the trabecular smooth muscle and vasodilation of the arterioles results in several-fold increase of blood flow, which expands the sinusoidal spaces to lengthen and enlarge the penis. The expansion of sinusoids compresses the venular plexus against the tunica albuginea. In addition, stretching of the tunica compresses the emissary veins and thus reduces the outflow to a minimum.

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