

From Impotence to Erectile Dysfunction: Reflections on 50 Years in Male Sexual Medicine



HISTORY

Today erectile dysfunction (ED) is a commonly known medical condition with various effective therapies, but this was not always the case. When I was in medical school (1963-1968) this condition fell under a rubric called impotence. Our understanding of impotence and our ability to effectively manage it was almost nonexistent. The urology text used when I was a student had the following to say about impotence:

“Various degrees of impotence in men are common, but it is rare to find definite organic cause for the complaints, which include inability to gain an erection, weak erections, premature ejaculation, loss of libido, or loss of normal sensation with ejaculation. The cause of almost all of these difficulties is psychogenic.”

This text went on to say:

“...with few exceptions, the causes of sexual difficulties are psychic, i.e., based on guilt, anxiety, jealousy, or frigidity on the part of the wife... Many of these men are obviously tense and nervous... Unless the patient's difficulties are of short duration, he should be referred to a psychiatrist.”¹

Due to this poor understanding and lack of effective treatment, relatively few men presented with these complaints.

Seminal events in our understanding and ability to effectively treat these disorders are the following:

- Masters and Johnson—*Human Sexual Response* (1966)² and *Human Sexual Inadequacy* (1970)³
- Inflatable penile prosthesis implantation (1973)⁴
- Penile vasoactive drug injection (1983)⁵
- National Institutes of Health Consensus Conference on Impotence (1992)⁶
- Effective oral therapy, sildenafil citrate (1998)⁷

The following observations are based on 5 years of urology resident training followed by 45 years of practice in a urology subspecialty that has a high proportion of men with various forms of sexual dysfunction. Many of my observations are supported by references; those which are not should be regarded as solely my opinions.

WHAT IS ED?

I was part of the panel for the National Institutes of Health Consensus Conference on Impotence which convened in 1992. The most significant outcome of that conference was the panel's decision to abandon the term impotence and to redefine it as ED. ED was defined as the inability to attain or maintain an erection suitable for satisfactory intercourse on more than 50 percent of attempts.⁶

Primary ED is ED which exists from a man's first attempts to have intercourse. Most men with this disorder are otherwise healthy and primary ED is almost always due to psychological causes. Anxiety mediated through the sympathetic nervous system prevents complete corporeal smooth muscle relaxation; thus veno-occlusive dysfunction is the mechanism of psychogenic ED.⁸ Secondary ED is ED which develops after a well-established period of normal sexual function. In most of these cases there are significant underlying organic causes. Unless secondary ED develops after trauma or certain surgical procedures, there is a period of gradually decreasing erectile rigidity leading to the threshold where ED, according to the above definition, can be said to exist.

LIBIDO, ORGASM, AND EJACULATION

Apart from or along with ED men may also have decreased libido. Low or absent sexual desire may be due to a number of factors including depression, chronic illness, relationship conflict, alcohol abuse, low testosterone (hypogonadism), and medications. Some men who have ED may also experience low libido because of repeated failures.

Some men have difficulty or inability to reach climax. The reasons for this are also multifactorial including among others alcohol abuse and certain medications, especially antidepressants. Other men have dry orgasms either due to failure of seminal emission or retrograde ejaculation. Finally, there is premature or rapid ejaculation which the AUA (American Urological Association) Guideline Panel for Premature Ejaculation defines as “ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either 1 or both partners.”⁹ Premature ejaculation (PE) may be either primary, occurring since first sexual attempts with a partner, or acquired, occurring later in life. PE is the most common of the male sexual dysfunctions.¹⁰

From a reproductive standpoint, any ejaculation that occurs inside the vagina is appropriate; and in many animal species ejaculation occurs soon after intromission. To prolong pleasure men have learned to delay orgasm and ejaculation. This learning process usually takes place during adolescent masturbation with the recognition that

with respect to orgasm there is a point of no return. As this point approaches boys learn to slow self-stimulation thus prolonging pleasure and building confidence in their ability to achieve and maintain erections. When they later experience their first partner encounter, PE or the failure to maintain the erection is less likely to occur. Many of the young men I have seen with either primary PE or primary ED come from orthodox religious backgrounds which forbid masturbation or coitus before marriage. The complaint of lifelong PE appears also to be increasing because some young men have unrealistic expectations regarding ejaculatory control based on their exposure to internet pornography content. Primary PE and primary ED need careful consideration as some of these men often present with the complaint of ED when they actually have PE. They see short lasting erections as their main complaint not realizing that penile detumescence is normal after ejaculation. Treatment for men with either primary PE or primary ED is sex therapy which creates through behavior modification skills not learned through solitary masturbation.³

Secondary PE often occurs in the setting of early ED when the man can no longer slow down to avoid impending ejaculation because in doing so he will lose his erection. The AUA Guideline on Premature Ejaculation in this setting recommends that the ED be treated first.⁹

HOW COMMON IS ED?

The Massachusetts Male Aging Study is widely cited as evidence for ED prevalence. This longitudinal observation study of males between the ages of 40 to 70 found a prevalence of 52% for mild, moderate, and severe ED combined. The prevalence of severe ED within this study tripled from 5% to 15% between the ages of 40 and 70.¹¹

Does this mean that ED is a normal consequence of aging? Masters and Johnson pointed out that healthy men can remain sexually active for a lifetime. With age getting an erection requires more direct genital stimulation, following orgasm detumescence is faster, and the latency period (the time from an orgasm until a man can get another erection) is longer.² The increasing prevalence of ED with age in our society is the result of vascular disease, diabetes, and other disorders that increase with aging especially in men who make poor lifestyle choices. Poor diet, smoking, lack of physical activity and abuse of alcohol, metamphetamines, and opiates are included in these choices.

Men ask me what they can do to preserve their sexual function. A large part of ED is vascular, and so the good news is that what men should do to avoid cardiovascular disease will also help them to avoid ED. What do I and most medical professionals recommend in this regard?

- No smoking
- A heart healthy diet (Mediterranean is often cited)
- Regular aerobic and muscle strengthening exercise
- Maintain ideal body weight

- If necessary control hyperlipidemia, hypertension, diabetes mellitus
- Alcohol use in moderation or not at all and avoidance of illicit drugs

EVALUATING MEN WITH SEXUAL PROBLEMS

In general the evaluation of any medical problem follows this format: history, physical examination, then possible blood and urine tests, imaging studies, and sometimes specialized testing. The single most important element in evaluating men with sexual problems is a detailed history. In the 1970's a detailed history along with physical examination were the only evaluation tools available. With time specialized tests such as nocturnal penile tumescence studies,¹² diagnostic cavernous injection,¹³ dynamic infusion cavernosometry and/or cavernosography,¹⁴ and color duplex penile ultrasonography¹⁵ were developed. With the exception of nocturnal penile tumescence¹⁰ and the arterial phase of color duplex ultrasonography,¹⁶ these tests were not validated by applying them to controls (men without ED). In spite of this, many experts evaluating men with sexual problems came to rely on these specialized tests to the extent that important sexual history taking became abbreviated. Also leading to this shortening of sexual history taking was overreliance by some on inventories such as Sexual History Inventory for Men.¹⁷

The result in some cases can be illustrated by MW, a 24-year-old man I saw who had presented to another male sexual dysfunction expert with the complaint of ED existing since his first experience with a partner. Multiple studies were done leading to a diagnosis of ED due to vascular causes. A microsurgical inferior epigastric artery bypass to the dorsal penile artery was performed. In spite of the patency of the bypass, the patient's problem was unchanged, and he came to me for a second opinion. After taking the complete sexual history that should have been taken by the first expert, I found that this young man's problem was not primary ED but actually primary PE. Starting with his first sexual encounter, he always had an erection but ejaculated almost immediately after vaginal penetration. Like many young men with this problem, he viewed his problem as a failure to maintain his erection, not recognizing that loss of erection after ejaculation is normal. I referred him to a sex therapist for treatment of his PE and a successful outcome resulted.

The pioneering work of Masters and Johnson provided a greatly expanded knowledge about normal and abnormal sexual function in the male and female (1966),² and introduced sex therapy (1970)³ as a management technique. Sex therapy ideally involves both the man and his partner. For PE both the start-stop technique and the squeeze technique during manual penile stimulation are designed to help the man identify the point of no return and to learn as this approaches how to modify his behavior to delay orgasm. For difficulties obtaining and maintain erections associated with performance anxiety,

sensate focus exercises allow couples to gradually build confidence thereby overcoming this problem.

OTHER TREATMENT OPTIONS FOR MEN WITH ED

HL, a 49-year-old man, appeared on my schedule 1 day as an established patient. I had seen him for the first time 1 year previously when he presented with the complaint of a 2 year difficulty achieving and maintaining his erections. Over a period of several years he had gained weight and was 60 pounds over his ideal weight. He was taking medications for both hypertension and type 2 diabetes mellitus. At the conclusion of that first visit I discussed life style modifications, and I gave him a prescription for 6 sildenafil citrate (Viagra) 100 mg tablets with instructions on how to use them for a treatment trial. Because he lived in another state, I instructed him to call me; if the oral medication was effective, we would continue it. If it was not, we would explore other treatment options.

I had not heard from him and as I went into his examination room, I expected to continue what we had begun 1 year ago. When I asked him about the effectiveness of the sildenafil citrate, he stated that he no longer had ED. I assumed then that the medication had been effective, but it turned out that he was not taking it. What he had done instead was to accept my life style recommendations by adopting a Mediterranean diet along with 1 hour of brisk walking daily. In the ensuing year he lost 50 pounds, and his hypertension and diabetes medications were no longer necessary. In HL's case he had not been a smoker nor had he abused alcohol so changes there had not been necessary. The purpose of this second visit was to evaluate symptoms that turned out to be due to early benign prostate enlargement.

Men presenting with secondary ED may have underlying cardiovascular disease so evaluation and possible intervention in this regard by a primary care physician or a cardiologist is in order. For the person treating ED, life style modifications should be offered as a first time management whenever appropriate. In cases of long established ED they might not be as effective as they were in the case of HL; nevertheless, they are important in terms of the man's general health, and they can increase the effectiveness of oral medications for ED.

The issue of testosterone deficiency (hypogonadism) often comes up in part due to direct to consumer advertising describing in men low libido, lack of energy, day time sleepiness, weight gain, and ED as possible symptoms. Hypogonadism may be the cause in some of these cases but in my experience these symptoms are more likely the result of either physical deconditioning due to poor life style choices or depression.

The current AUA Guideline on ED recommends serum testosterone determination on all men presenting with ED.¹⁸ However, if a man with ED has normal libido and no constitutional symptoms suggesting possible hypogonadism,

I do not order a serum testosterone. In cases where serum testosterone determination is indicated, the blood draw because of diurnal testosterone variation should be done in the early morning. If the serum testosterone is low, the test should be repeated along with serum LH and prolactin. If hypogonadism is confirmed, it should be determined whether it is primary (testicular failure) or secondary (hypothalamic-pituitary dysfunction) and then managed appropriately. In my experience, however, hypogonadism is not a common factor in the many men I see with secondary ED.^{10,19}

After the above considerations, the first line of treatment for most men with secondary ED is a trial of one of the oral type 5 phosphodiesterase inhibitors (sildenafil [Viagra], tadalafil [Cialis], vardenafil [Levitra], or avanafil [Stendra]). Many men are able to manage their ED with one of these drugs for a while, but it is not unusual if life style changes are not made for these medications to eventually lose their effectiveness as the underlying factors causing ED progress. Men who have anal sex need firmer erections and PDE-5 inhibitors often are insufficient in this regard. Young veterans returning from conflict face special problems including altered family dynamics, closed head injuries, post-traumatic stress disorders, and genital trauma. Collaboration between sexual medicine physicians and their colleagues in psychology are needed to provide a holistic approach to men with these complex problems.

Previously, second-line treatment options after oral medication failure included the use of a vacuum erection device, urethral suppositories, and vasoactive drug injections into the penile erection chambers (corpora cavernosa). Only after these second line options were found to be unsatisfactory or rejected was third-line treatment (penile prosthesis implantation) considered. Today many, including myself, include penile prosthesis implantation in the second-line treatment option discussion; and it is not unusual for a man to progress from oral medication treatment failure directly to a penile prosthesis.

PEYRONIE'S DISEASE AND ED

Although it was first described by Fallopius in 1561, Peyronie's disease (PD) bears the name of Francois de la Peyronie who described it in a case report in 1743.²⁰ PD is characterized by palpable abnormalities in the penis variously described as plaques, nodules, or scar, and it is associated with deformed erections and penile shortening. PD has been frequently linked to ED but how often and which comes first has been in dispute.²¹ Devine, et al in 1997 suggested that poor rigidity during intercourse may lead to delaminating injuries of the elastic covering (tunica albuginea) of the penile erection chambers (corpora cavernosa).²² These injuries heal with scar formation which leads to PD. This is a common condition in men ages 40-75 with a prevalence of almost 9%.²³

As mentioned previously, most men with secondary ED have a period of gradually decreasing erectile rigidity

preceding their ED. If normal erectile rigidity in a young man is 10/10, men with rigidity of 6 or 7/10 are able to penetrate hence they have not reached the threshold of having ED. It is during this time however that they are subject to the thrusting injuries described by Devine. The forces involved are not great and pain at the time of injury is not always present. In addition these injuries may be recurrent. In my experience only one-third of men have a history of painful intercourse before the onset of PD. Young men with 10/10 erections seldom damage their penises during intercourse; however, if the force involved is great, there is sudden sharp pain following by detumescence, swelling, and ecchymosis. This condition is known as penile fracture. During surgical repair a complete tear in the tunica albuginea is found usually at the penile base. It is easy to understand that in men who are able to have coitus but with decreased penile rigidity, the forces needed to cause only partial disruption of the tunica albuginea are not great; and that the injuries may be silent, recurrent, and further out on the penile shaft.

I have suggested that we call this prodromal phase of decreased penile rigidity leading up to ED erectile insufficiency (EI). If one includes EI with ED, I postulate that EI/ED precedes PD and is not a complication of PD but rather its cause.^{24,25}

Returning to the consensus conference definition of ED, the inability to attain or maintain an erection suitable for *satisfactory* intercourse on more than 50 percent of attempts, *satisfactory* refers to the ability to initiate and complete the act. However, *satisfactory* intercourse should also mean intercourse that does not cause penile injury (a new definition for safe sex).²⁵

For men who are still having penetrative sex but with erections of decreased rigidity (EI), measures to decrease the probability of PD or its recurrence might be possible. To do this an Owner's Manual for the Penis² might provide the following suggestions:^{24,25}

- Oral medications for ED (PDE5 inhibitors) are generally not prescribed until men have ED. Earlier use in men with EI might produce erections with better rigidity and maintenance.
- Adequate lubrication should be present or a lubricant should be used.
- The man or his partner should use their hand to guide the penis in or back in if it slips out.
- Partner on top positions should be avoided.
- Penile thrusting straight in or out is permissible but placing torque on the penis should be avoided.
- Finally, penetrative sex should be avoided when the man is fatigued or has had too much alcohol to drink.

Men with PD who can still have penetrative sex should be provided with these Owner's Manual suggestions to prevent recurrent injuries. If erectile deformity is great enough to impede intromission or to make it uncomfortable, the goal should be to straighten the penis without further reducing erectile function. Penile plication does

this by making the normal side of the penis the same length as the shortened scarred side and does so without impeding erections.²⁶ Removing the penile plaque and replacing it with a graft entails significant risk of reduced erectile function,²⁷ and consequently many including myself are avoiding the routine use of this option recognizing that graft surgery is still sometimes necessary. Injections of clostridial collagenase into the plaque can improve deformity, but usually only partially, and this treatment does nothing to improve the ability to attain or maintain erections.²⁸ Consequently, I prefer penile plication as a straightening measure if the man's EI is mild. If a man being considered for plication has EI or mild ED and he does not respond to PDE5 inhibitors, then penile prosthesis implantation should be considered. Today's 3 piece inflatable prostheses provide reliable erections, and when inflated the cylinders usually correct the deformity. We showed that if there is residual deformity after the device is inflated, modeling (bending the penis with the cylinders inflated) almost always takes care of the rest.²⁹ Although this initial observation was based on a small sample size, our observations have remained the same after many additional implants in men with PD.

MORE ABOUT PENILE PROSTHESIS IMPLANTATION

After the introduction of the inflatable penile prosthesis in the 1970's, sex therapy and penile prosthesis implantation were the only available management options for men with ED. Despite the advent in ensuing years of other nonsurgical options, penile prosthesis implantation still plays an important role in the management of ED because it is almost always effective when other options are not or when other options are rejected by the man and his partner. Most men can experience orgasm and ejaculation without erection, and penile prosthesis implantation does not take this away hence its popularity.

The ideal penile prosthesis would not be apparent and would produce flaccidity and erection which come as close as possible to what is produced by natural mechanisms. The 3 piece hydraulic inflatable devices come closest in this regard, and they are the most popular devices in United States. In a 3 piece device the paired expandable cylinders which are placed in the corpora cavernosa are 1 piece, the small scrotal pump with a deflation mechanism is the second piece, and the third piece is the large abdominal fluid reservoir.

Success rates in penile prosthesis surgery are high however when the surgery goes well but the patient is not satisfied, then proper expectations were either not conveyed to the patient or they were but they were not understood or embraced by him. The most common reason for dissatisfaction in my experience is that the patient is disappointed that his penis and the erection provided by the device are shorter than what he was expecting. Second in line is the lack of glans tumescence; a penile prosthesis cannot supply this. Both penile shortening and lack

glans tumescence should be included in the preoperative discussion.

How much shorter will the erection be after penile prosthesis implantation? The bulk of the penis length and girth is supplied by the paired erection chambers (corpora cavernosa). The corpora have an elastic outer covering (tunica albuginea) with inner circular and outer longitudinal fibers. These chambers are filled with smooth muscle. A third chamber in the penis (the corpus spongiosum) lies in the midline beneath the corpora; it surrounds the urethra and at its end it forms the glans penis which sits like a cap on top of the tips of the corpora cavernosa. Many men with organic ED have a penis which, while it no longer erects normally, nevertheless is structurally grossly normal. The expected length of their penis with the prosthesis inflated is fairly close to the stretched length of their flaccid penis prior to surgery. This is somewhat less than the length of their previously normal erection. Other men, however, have lost penile length due to various factors (see next section), and their flaccid penis may have limited stretch. The erection produced by a prosthesis in these men is similar in length to their stretched penis, and this stretched length is much shorter than it used to be and so is the erection.

RETURN OF THE FORESKIN

Circumcision status is often important in men with penis problems. In their examination notes most urologists note whether a man is circumcised or uncircumcised based on the appearance of the man's penis while he is supine on the examination table. Some men who were circumcised earlier in life may later have the appearance of being uncircumcised. I call this "Return of the Foreskin." Return of the foreskin means that penile shortening has taken place and conditions causing this include:

- Radical prostatectomy
- Peyronie's disease (fibrosis of the tunica albuginea)
- Abdominal obesity
- Fibrosis of the corporal smooth muscle

After ischemic priapism

After removal of an infected penile prosthesis

Following radical prostatectomy (complete removal of the prostate and seminal vesicles), many men lose penile length (most commonly about 1 inch).³⁰⁻³² PD results in scarring of the tunica albuginea leading to a shorter and deformed erect penis. While deformity (curvature) can be corrected, restoration of lost penile length is not possible.

The penis itself has a portion, the shaft, which is outside the body, as well as another portion attaching to the pelvis inside the body. When we implant a penile prosthesis through an incision at the junction of the penis and scrotum, 2 cm openings are made in the corpora. A measuring rod placed in the corpora determines the length distally (toward the glans) and then proximally (toward the pelvic bone attachments). These measurements determine cylinder size. On 1 particular day I had 2 men undergoing

penile prosthesis implant procedures. Both had total corporal lengths (proximal plus distal) of 18 cm. In the first man with a BMI of 23, the distal measurement was 12 cm, and the proximal measurement was 6 cm. In the second man with a BMI of 36, the distal measurement was 6 cm, and the proximal measurement was 12 cm. In the thin man, two-thirds of his penis was outside his body, and in the obese man two-thirds of his penis were inside his body. These 2 cases illustrate that abdominal obesity is another cause of apparent penile shortening. Obese men with this problem are sometimes said to have a "buried penis." In obese men who lose significant weight, more of the penis emerges from the body.

Ischemic priapism is a persistent nonsexual induced erection. After several hours oxygen is depleted from the blood trapped in the corporal bodies, and the erection becomes very painful. The corporal smooth muscle suffers ischemic damage, the erection eventually subsides, and the damaged smooth muscle is replaced by scar. Men with ED following ischemic priapism usually can only be successfully treated by penile prosthesis implantation. Smooth muscle fibrosis also results following removal of an infected penile prosthesis; and only repeat penile prosthesis implantation will effectively treat this ED. While implanting an inflatable penile prosthesis is often the only effective treatment for men with corporeal fibrosis, placing penile prosthesis cylinders into fibrotic corpora can be challenging sometimes requiring special techniques such as corporeal excavation.³³

BACK TO PREMATURE EJACULATION

As discussed previously primary PE can and ideally should be treated by a sex therapist. Patients however often resist the suggestion of referral to a sex therapist because this may not be covered by their health plan, it requires multiple visits, they might be reluctant to involve their partner, and also because they simply would rather take a pill.

Men treated for depression with certain antidepressants sometimes experience inability to reach orgasm. This observation led to the off label use of lower doses of these agents to treat PE in men who do not have depression, and while these medications have been shown to produce a statistically significant increase in the time to ejaculation (ejaculatory latency), this increase is not always clinically significant in terms of the patient's and partner's satisfaction. In addition, side effects (nausea, drowsiness, and dry mouth) may be bothersome. Another treatment for PE is application of an anesthetic ointment to the penis. This works by decreasing sensation for the man, and this along with possible transmission to the partner limit the effectiveness of this management tool.

WHAT ABOUT FEMALE SEXUAL DYSFUNCTION?

While Masters and Johnson in their book *Human Sexual Response* (1966)² addressed both female and male sexual response issues, and in their book *Human Sexual*

Inadequacy (1970)³ proposed sex therapy techniques for both sexes, much of the early subsequent attention of the medical profession has been directed to sexual problems in men not women. Why is this?

We discussed at the beginning the poor understanding of male problems in the 1960's as well as the lack of effective treatment options. Among the male sexual dysfunctions ED is unique in that most men suffering from ED are able to have an orgasm and in most cases ejaculate. Many of these men have normal libido. Thus any treatment for ED that makes coitus possible would be very effective. Early penile prostheses had been developed for this purpose, but they were single, rigid rods implanted not inside the corpora but under the fascia only in the penile shaft.^{34,35} These devices did not work well and few were implanted.

Dr. F. Brantley Scott, Dr. William E. Bradley, and Dr. Gerald S. Timm set out in to find a solution to severe urinary incontinence. In doing so they developed the artificial urinary sphincter.³⁶ This was a silicone hydraulic device; and the initial model had 2 pumps, a sphincter cuff, and a fluid reservoir. As they were bringing the artificial sphincter to market, they considered the possibility that the same technology could be used to develop an inflatable penile prosthesis,⁴ and they then proceeded to develop this device. Once the inflatable penile prosthesis became available, urologists started implanting it with good results, and finally an effective treatment for male ED was available. For years this was the only treatment other than sex therapy for ED, and urologists needed to learn how to take a sex history so that they were offering this new treatment appropriately.

In 1983 Dr. Giles Brindley, a British psychiatrist and physiologist, hypothesized that an injection of phenoxybenzamine, a smooth muscle relaxant, into the penile corpora might produce an erection. He used himself as an experimental subject with good results, and this opened up both diagnostic testing and now an alternative therapy for ED.⁵

For years many oral medications to treat ED had been tried but with no real success. A new class of vasodilator medications (phosphodiesterase inhibitors) emerged, and one of these was being evaluated by Pfizer in the United Kingdom as a possible new treatment for angina pectoris. The hope was that this drug would not only be more effective than existing agents but also have fewer side effects. During the clinical trial it was apparent that it was effective and its side effect profile was acceptable, but it was not that much better than existing medications so the clinical trial was halted. When study participants were asked to return their numbered vials, many of the men who had been randomized to receive the active agent rather than placebo asked "what's going to happen to my erections?" Pfizer took this agent, sildenafil citrate, back to the drawing board; and after new clinical trials it was given the brand name Viagra and brought in 1998 to Europe and US markets to treat ED.⁷

What is apparent is that ED, while it is not the most prevalent male sexual dysfunction, (PE is),¹⁰ it is almost as prevalent and it is the most treatable of all the male sexual problems. The seminal events in the treatment of ED came about largely by serendipity and this has not happened in the female sexual dysfunction arena. It was only after investigation into the mechanisms of female sexual dysfunction and the development of a classification system that progress in this arena began.³⁷ Significant progress is now emerging, for example there are now 2 FDA approved medications for the enhancement of female hypoactive sexual desire disorder,^{38,39} and it is expected that this progress will continue.

Drogo K. Montague

Department of Urology, Glickman Urological and Kidney
Institute, Cleveland Clinic, Cleveland, OH
E-mail: montagd@ccf.org

References

1. Smith DR. *Urology*. 5th ed. Los Altos, CA: Lange Medical Publications; 1966.
2. Masters WH, Johnson VE. *Human Sexual Response*. Boston: Little Brown and Company; 1966.
3. Masters WH, Johnson VE. *Human Sexual Inadequacy*. Boston: Little Brown and Company; 1970.
4. Scott FB, Bradley WE, Timm GW. Management of erectile impotence: use of implantable inflatable prosthesis. *Urol*. 1973;2:80–82.
5. Brindley GS. Cavernosal alpha-blockade: a new technique for investigating and treating erectile impotence. *Br J Psychiat*. 1983;143:332.
6. NIH. Consensus panel on impotence: Impotence. *JAMA*. 1993;270:83–90.
7. Goldstein I, Lue TF, Padma-Nathan H, et al. Oral sildenafil in the treatment of erectile dysfunction. Sildenafil Study Group. *N Engl J Med*. 1998;1339:1397–1404.
8. Reed-Maldonado A, Lue TF. A syndrome of erectile dysfunction in young men. *Transl Androl Urol*. 2016;2:228–234.
9. Montague DK, Jarow J, Broderick GA, et al. AUA guideline on the pharmacologic management of premature ejaculation. *J Urol*. 2004;172:290.
10. Rosen RC. Prevalence and risk factors of sexual dysfunction in men and women. *Curr Psychiat Rep*. 2000;2:189–195.
11. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol*1094;151:54–61.
12. Karacan I, Scott FB, Salis PJ, et al. Nocturnal erections, differential diagnosis of impotence, and diabetes. *Biol Psychiatry*. 1977;12:373–380.
13. Virag R, Frydman D, Legman M, et al. Intracavernous injection of papaverine as a diagnostic and therapeutic method in erectile failure. *Andrology*. 1984;35:79–87.
14. Montague DK, Lakin MM, VanderBurg Mendendorp S, et al. Infusion pharmacocavernosometry and nocturnal penile tumescence findings in men with erectile dysfunction. *J Urol*. 1991;145:768–771.
15. Altinkilic B, Hauck EW, Weidner W. Evaluation of penile perfusion by color-coded duplex sonography in the management of erectile dysfunction. *World J Urol*. 2004;22:361–364.
16. Broderick GA, Arger PA. Penile blood flow study: age specific reference ranges. *J Urol*. 1994;151:A371.
17. Rosen RC, Cappelli JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res*. 1999;11:319–326.
18. Burnett AL, Nehra A, Breau RH, et al. Erectile dysfunction: AUA Guideline. *J Urol*. 2018;200:633–641.

19. Buvat J, Bou Jaoude G. Significance of hypogonadism in erectile dysfunction. *World J Urol.* 2006;6:657–667.
20. Jordan GH, McCammon KA. Peyronie's disease. In: Wein, Kavoussi, Novick, Partin, Peters, eds. *Campbell-Walsh Urology.* 10th ed. Philadelphia: Elsevier Saunders; 2012.
21. Chiles K, Mulhall JP. Peyronie's disease: prevalence, pathophysiology, and evaluation. AUA Update Series. Series 32: lesson 6.
22. Devine CJ, Somers KD, Jordan SG, et al. Proposal: trauma as the cause of Peyronie's disease. *J Urol.* 1997;17:285–290.
23. Mulhall JP, Creech SD, Boorjian SA, et al. Subjective and objective analysis of the prevalence of Peyronie's disease in a population of men presenting for prostate cancer screening. *J Urol.* 2004;157:2350–2353.
24. Montague DK. Peyronie's disease and erectile dysfunction: a new perspective-what every urologist and man should know about Peyronie's disease. *J Genital Surg.* 2017;1. Article 2 online open access.
25. Montague DK. New perspectives into Peyronie's disease: etiology, management, and prevention. *Urol.* 2019;125:6–7.
26. Daitch JA, Angermeier KW, Montague DK. Modified corporoplasty for penile curvature: long-term results and patient satisfaction. *J Urol.* 1999;162:2006–2009.
27. Kim DH, Lesser TF, Aboseif SR. Subjective patient reported experiences after surgery for Peyronie's disease: corporeal plication versus plaque incision with vein graft. *Urol.* 2008;71:698–702.
28. Gelbard M, Goldstein I, Hellstrom WJ, et al. Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of peyronie disease in 2 large double-blind, randomizes, placebo controlled phase 3 studies. *J Urol.* 2013;190:199–207.
29. Montague DK, Angermeier KW, Lakin MM, et al. AMS 3-piece inflatable penile prosthesis implantation in me with Peyronie's disease: comparison of CX and Ultrex cylinders. *J Urol.* 1996;156:1633–1635.
30. Savoie M, Kim SS, Soloway MS. A prospective study measuring penile length in men treated with radical prostatectomy for prostate cancer. *J Urol.* 2003;169:1462–1464.
31. Mulhall JP. Penile length changes after radical prostatectomy. *BJU Int.* 2005;96:472–474.
32. Gontero P, Galzerano MR, Bartoletti R, et al. New insights into the pathogenesis of penile shortening after radical prostatectomy and the role of postoperative sexual function. *J Urol.* 2007;178:602–607.
33. Montague DK, Angermeier KW. Corporeal excavation: a new technique for penile prosthesis implantation in men with severe corporeal fibrosis. *Urol.* 2006;67:1072–1075.
34. Pearman RO. Treatment of organic impotence by implantation of a penile prosthesis. *J Urol.* 1967;97:716.
35. Lash H. Silicone implant for impotence. *J Urol.* 1968;100:709.
36. Scott FB, Bradley WE, Timm GW. Treatment of urinary incontinence by implantable prosthetic sphincter. *Urol.* 1973;1:252–259.
37. Basson R, Berman J, Burnett A, et al. Report of the international consensus development conference on female sexual dysfunction: definitions and classifications. *J Urol.* 2000;163:888–893.
38. Joffe HV, Chang C, Sewell C, et al. FDA approval of fibanserin – treating hypoactive sexual desire disorder. *NEJM.* 2016;374:101–104.
39. Althof S, Derogatis LR, Greenberg S, et al. Responder analyses from a phase 2b dose-ranging study of bremelanotide. *J Sex Med.* 2019;16:1226–1235.