

Managing Erectile Dysfunction – A Patient Guide

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Greetings!

These guidelines are designed to provide patients with Erectile Dysfunction (ED) and their partners information and advice on the condition. We hope that this information will give you confidence to address any erectile problems you may experience, no matter the cause. For some people, this information will be completely new, while others may be well informed about ED and its treatment options. For many patients, much of what is discussed herein may be familiar. Either way, don't feel that this material has to be fully absorbed in one sitting. It may be helpful to review the information presented with your health care provider(s) to adapt the recommendations to fit your needs. We would be grateful if you could fill out the questionnaire at the end of the booklet and return it to us with your feedback to improve the experience for future patients.

You can e-mail your comments to urologyresearch@UCSF.edu or mail them to Your Health Matters Box 1695, UCSF Department of Urology, San Francisco, CA 94143-1695.

If you would like to discuss the various treatment options, UCSF has medical professionals and patients available to speak with you. To talk with a medical professional, contact the UCSF Department of Urology at Parnassus Heights at (415) 353-2805 To receive the contact information for a patient who has had an erection problem and tried available aids, contact the UCSF Helen Diller Family Comprehensive Cancer Center's Resource Center at (415) 885-3693.

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Introduction

Erectile Dysfunction, or ED, is defined as difficulty or inability to attain and maintain an erection sufficient for satisfactory sexual activity. ED is a relatively common problem, affecting up to 30 million people of all ages in the United States, and over 150 million people worldwide. The ability to have an erection requires complex coordination of nerves, blood vessels, muscles, and the brain.

ED is also a side effect of many medications. Neurological, vascular, and/or hormonal issues may contribute to or cause ED. Psychological issues (e.g., depression, anxiety, performance concerns) are also quite prevalent and play at least some part in virtually every case of ED. Our goals with this Patient Guide are to explain how penile erection is achieved, what conditions may cause ED, and how to effectively manage the condition.

What is ED?

Sexual function has traditionally been thought of as a linear process; sexual interest or desire is the first phase which often leads to penile erection (the penis goes from being flaccid to very firm or erect due to blood flow). After a period of sexual excitement/activity most people experience ejaculation (release of semen from the penis) which is accompanied by orgasm, a sensation of intense pleasure and/or contentment. It is important to note that orgasm and ejaculation are separate processes that may occur independently. It is also possible to experience ejaculation and/or orgasm in the absence of penile erection.

Decreased sexual desire, also referred to as decreased libido, is common and may occur in the setting of psychological distress (depression/anxiety), stress, and relationship conflict. Some health problems are associated with decreased desire. Decreased sexual desire has also been associated with low blood levels of testosterone, the “male hormone.”

Erectile dysfunction – commonly known as ED – is defined as the inability to achieve or maintain an erection that is sufficient for satisfactory sexual activity. Ejaculation, the release of semen during sexual activity, relies on coordinated action of the muscles of the lower urinary tract and prostate. The prostate and the seminal vesicles produce most seminal fluid. Medications, surgeries, and radiation treatments for prostate problems often cause changes in ejaculation (e.g. decreased volume and consistency.) Ejaculation changes are also common with increasing age.

Orgasm occurs as an experience of intense physical and emotional pleasure at the climax of sexual activity. Our current scientific understanding of the experience of orgasm is limited. Many factors, including emotional, psychological, and health considerations may contribute to the experience of orgasm. Changes in ejaculation may also influence the perception of orgasm in some, and others may experience ejaculation but have a mild or even no sensation or orgasm.

It is important to realize that sexual function is not simply the ability to have a rigid erection and/or an ejaculation. A careful assessment of sexual life and the quality of the sexual relationship are important to produce the best outcomes when addressing any type of sexual problem. It is also important to remember that mutually satisfactory sexual relationships can be maintained in the presence of ED or other sexual problems. For more information about this, refer to the books listed at the end of this guide.

ED is common with age and in the presence of other medical conditions

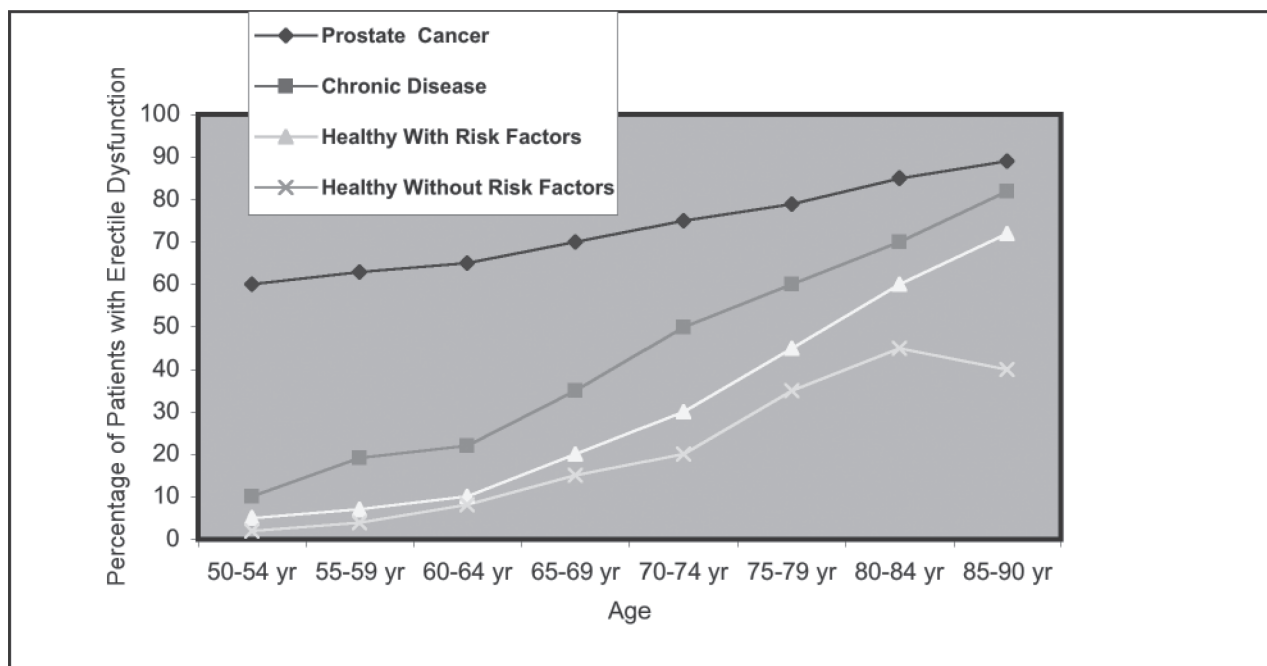


Figure 1: Prevalence of Erectile Dysfunction with Age in Different Patient Populations.

Chronic disease includes other cancer, hypertension, cardiac disease, diabetes or stroke.

Risk factors for ED include chronic vascular diseases (high blood pressure, diabetes, high cholesterol), tobacco use, obesity, lack of exercise, neurologic injury, and hormone deficiency.

Data from *Ann Intern Med.* 2003 Aug 5; 139(3): 161-8. Printed with Permission from the American College of Physicians

ED and Cancer Surgery or Radiation

ED is very common after major pelvic surgery or radiation, including treatments for prostate or bladder cancers. It is the most common side effect of prostate cancer surgery and radiation treatments. The nerves that drive erection, called cavernous nerve bundles, are located immediately next to the prostate gland (See Figure 2). During a radical prostatectomy (RP, an operation for prostate cancer) these nerves may be injured. This typically causes ED that is, in many cases, at least partially permanent. Because the prostate makes most of the fluid in semen, patients who have had RP do not experience ejaculation.

Radiation to the prostate, the bladder or rectum can also damage the cavernous nerves and lead to problems with erections and ejaculation. These effects tend not to be immediate but often manifest within a few years after treatment is completed. Although ED and absence of ejaculation are common after RP or prostate radiation, sexual desire and the ability to achieve orgasm are still possible.

A “nerve-sparing” RP or radical cysto-prostatectomy (RC, an operation for bladder cancer) is a procedure designed to remove cancer while preserving one or both of the cavernous nerve bundles. Radiation oncologists have also developed “nerve sparing” radiation protocols by more precisely targeting radiation to the prostate. The nerve sparing approach is markedly superior to the older non-nerve sparing approach. While the nerve sparing does preserve the possibility of penile erections, most patients who have even nerve sparing surgery will experience a decline in erectile function that will partially, but may not completely, recover over two to three years following the operation. Newer techniques of “focal ablation” where only the cancerous region of the prostate is treated (usually by applying high or very low temperatures), sparing the rest of the gland, may be associated with lower risks of ED. Nerve sparing surgeries/radiation are often an option but may not

be appropriate for some cases of large and/or high-grade tumors. Patients with medical problems (e.g., high blood pressure, high cholesterol, diabetes, tobacco use), those who experienced ED prior to surgery/radiation, and older patients are more likely to have difficulty obtaining a rigid erection after even nerve sparing surgery/radiation. Depression, psychological stress, and relationship conflict may also make recovery more difficult by affecting both sexual desire and penile erection.

Patients who are receiving hormone blockade as part of their treatment for prostate cancer often experience reductions in libido and more severe difficulties with erections. After cessation of hormone blockade, testosterone production can recover for many patients, but this may take months or years. The likelihood of irreversible effects is related to patient age, pre-treatment sexual function, and the length of time hormone therapy is given.

Penile rehabilitation is a strategy for optimizing erectile function outcomes after treatment of prostate or bladder cancer with surgery and/or radiation. This approach is based on the theory that lack of blood flow and erections after cancer treatment will lead to scarring and shrinkage of the penis. In this context, even if the nerves recover over time, changes to the penis itself may make erections difficult. Theoretically, if blood flow to the penis can be maintained the tissue may be less prone to scarring and shrinkage.

The most common form of penile rehabilitation involves use of oral medications and/or devices to help stimulate blood flow and erection. The bulk of evidence supporting this practice comes from animal studies and small case series. However, the largest randomized placebo-controlled studies (the highest level of scientific evidence) of routinely dosed oral ED medications versus sugar pills (placebo) after prostate surgery have not demonstrated a significant improvement in likelihood of spontaneous erections returning. The AUA (American Urological Association) Guidelines on Erectile Dysfunction recommend that treating providers inform their patients that there is no compelling evidence that penile rehabilitation with oral medications works to restore spontaneous erection responses. Although these pills may not restore “natural” erections, they are effective in many cases as a short term “on demand” therapy to help stimulate erections, even after prostatectomy.

Many providers and patients still advocate routine use of oral meds for ED since this is generally safe and can help patients stay committed to recovery of their sexual quality of life. Use of the medications may also help during sexual encounters, even if they do not “restore” normal erectile function fully. Attention to vascular health (e.g., exercising, eating a sensible diet) and maintaining intimacy with one’s sexual partner is also a critical component of penile rehabilitation.

Treatment of ED

Treatment for ED will depend on an assessment of the patient and possible underlying cause(s) of the ED, including patient age, health and patient and provider preference. Most often, providers recommend a stepwise approach starting with the least intrusive option. There are a number of medical options that can help patients attain and maintain a rigid penis for sexual activity. While a stepwise approach from simple to more complicated treatments is appropriate for most patients, some patients may choose to “skip” or avoid some of the available treatment options. In the end, the goal is always to re-establish sexual intimacy and pleasure, which can be achieved in a number of ways. It is up to each individual patient to discuss priorities with their provider to make the right decision.

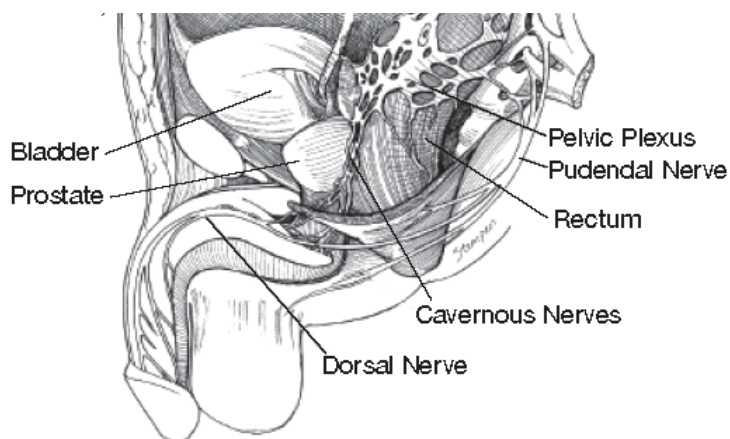


Figure 2: Nerves of the Pelvis. Note the close relationship of the prostate to the cavernous nerves (nerves that allow erection)

Coping with Erectile Dysfunction

Treatments for ED are very effective but do not work in every case. Patients may avoid certain treatments all together for a variety of reasons.

For patients in whom acceptable treatments for ED are not effective or acceptable, options remain for sexual intimacy and pleasure. Patients who are unable to achieve a rigid erection may still enjoy cuddling, genital caressing, and/or oral sex. With a supportive partner, patience, and a willingness to explore different means of being sexual, most patients are able to achieve sexual satisfaction and orgasm, regardless of whether they can obtain an erection sufficient for penetrative sex.

A good way to resume your sex life is to be open and use a gradual, progressive approach and to ensure that you and your partner feel comfortable at every step. Sensual, mutually pleasuring activities with no performance goal can allow you to be intimate in a relaxed way.

It may be necessary for sexual partners to redefine a sexual relationship after cancer treatment. . Although some may see kissing, caressing, and/or oral sex as simply foreplay in preparation for intercourse, arousing each other and even reaching orgasm without intercourse can be an important component of intimacy and a common way to share physical pleasure and emotional closeness without the need for a rigid erection. Your sex life should be based on what you and your partner mutually define as sexually satisfying and pleasurable, which may or may not include penile penetration. Vibrators have been used effectively by many patients to achieve orgasm.

Patients often overestimate their partner's feelings on the importance of penetration. Though penetration is an important part of many couples' sexual life and there are a number of medical options available to help achieve a rigid erection for penetration, it is important to focus on mutual pleasure and intimacy, not erectile hardness, in situations where an erection is not achievable or sustainable.

If you would like access to sexual or marriage counseling/advice, please ask your provider for a referral.

The American Association of Sex Educators, Counselors, and Therapists (www.aasect.org) and the Society for Sex Therapy and Research (www.sstarnet.org) maintain websites that contain valuable information on sexual wellness and searchable lists of credentialed experts on sexual wellness.

Table I: Treatment for ED

| Type of Therapy | Advantages | Disadvantages |
|--|--|---|
| Oral Medication (Viagra®, Levitra®, Cialis®, Stendra®) | <ul style="list-style-type: none"> • Pills taken by mouth • Effective in many patients | <ul style="list-style-type: none"> • Not always effective in patients who have prostatectomy, particularly when a non-nerve-sparing approach is used. • May take 30-120 minutes for full effect • Requires sexual stimulation to be effective • Potential side effects include headache, flushing, stomach upset, muscle pain • Should not be taken with certain medications, especially any sort of nitrate medication (e.g. nitroglycerin tablets, isosorbide dinitrate) which are commonly taken for chest pain or heart problems (see also table II) |
| Medicated-Urethral Suppository for Erections (MUSE™) | <ul style="list-style-type: none"> • Small pellet placed in the urethra • Few systemic side effects | <ul style="list-style-type: none"> • Can cause pain and/or burning sensation • Requires training • Refrigeration required • Side effects include (rarely) painful and prolonged erection of more than six hours, fainting, dizziness, pain or burning for the sexual partner |
| Penile Injections | <ul style="list-style-type: none"> • Highly effective • Few systemic side effects • Works in 5-10 minutes | <ul style="list-style-type: none"> • Some medications require refrigeration • Requires injection into the penis • In-office training is preferred • Can cause penile pain • Can cause prolonged erection • Theoretical risk of penile scarring |

| | | |
|-------------------|---|---|
| Vacuum Device | <ul style="list-style-type: none"> • No systemic side effects • Potentially low cost as it is a one-time purchase | <ul style="list-style-type: none"> • Can cause numbness or bruising • Erection sometimes described as “less natural” • Requires the use of a tight ring at the base of the penis • Some may find the device awkward to use |
| Penile Prosthesis | <ul style="list-style-type: none"> • Highly effective • Can be activated and deactivated in seconds | <ul style="list-style-type: none"> • Requires anesthesia and surgery • Small risk of infection that requires removal • Mechanical device can be an adjustment and may eventually stop working, requiring replacement surgery • The penis tends not to be as long as “natural” erections |

Oral Medications

Four oral medications are commercially available in the United States for the treatment of ED: sildenafil (Viagra®), tadalafil (Cialis®), vardenafil (Levitra®), and avanafil (Stendra®). These medications improve erections by working locally on the penis by inhibiting an enzyme called phosphodiesterase-5 (PDE-5). Following sexual stimulation, a compound called nitric oxide is released at the nerve terminals causing relaxation of penile smooth muscles. This occurs via a sequence of events beginning with nitric oxide and involves a compound cyclic guanine monophosphate (cGMP). cGMP helps blood vessels to stay open and maintains penile blood flow to keep an erection strong. PDE-5 breaks down cGMP and returns the penis to a flaccid state. All four of the ED medications currently available work by blocking the action of PDE-5, causing an increase in the level of cGMP levels in the penis. In the absence of sexual stimulation or in cases where there has been injury to the cavernous nerves, nitric oxide production may be minimal, and these medications will have little effect on the penis. These oral agents must be followed by sexual stimulation in order to achieve the desired erection.

Compared to patients taking a “placebo” of an inactive or sugar pill, those taking PDE-5 inhibitors report a higher satisfaction rate in overall sexual function, orgasm, penile rigidity and maintenance of erections. The likelihood of patient response to the aforementioned medications hovers around 70 to 80 percent, and is dependent on age, health and other factors (see above).

Oral medications have been used as a form of penile rehabilitation for patients who have undergone radical prostatectomy, radiation therapy, and hormone therapy. The theory underlying the use of these medications is that enhanced blood flow may help to spur recovery of spontaneous erections by keeping the penile tissues supplied with blood. As detailed above, existing evidence does not indicate that use of these drugs will help stimulate recovery of spontaneous erections after prostate cancer surgery but there is little harm from judicious, routine use of oral treatments for ED. Short-term enhancement of erectile response from use of these medications may help to facilitate sexual encounters and maintain intimacy while a patient is in recovery from prostate cancer treatment.

Viagra and Levitra remain in the blood stream and can help patients achieve erections for about 6–8 hours. Cialis is a long-acting medication which may exert an effect over 36 hours. Stendra stays in the circulation for a period of time somewhere between the Cialis and the other drugs. Studies show that all four drugs are generally well-tolerated with few side effects. No convincing evidence indicates that any one of these is “better” than the others although individuals may have personal preferences.

Patients at risk for heart attack or stroke should consult with their providers before engaging in sexual activity as exertion during sex can be a strain on the heart. Patients who are taking nitrate medicines should not take any PDE5 inhibitors as the combination can cause a severe drop in blood pressure that could be life-threatening. Caution should also be exercised in patients who are taking alpha blocker medications, which are commonly used for prostate problems and/or for high blood pressure, as there is a small potential for drop in blood pressure from taking both medications at the same time. Doses should ideally be separated by at least 4 hours.

Table II: Oral Medications

| How to take Oral Medications (Viagra/Levitra/ Cialis) | |
|--|---|
| Viagra | <ul style="list-style-type: none"> • Take 25-100 mg of Viagra one hour before you are ready to engage in sexual activity • Viagra works best 30 minutes to four hours after taking the pill • Viagra works best on an empty stomach. Do not take Viagra after a high-fat meal |
| Levitra | <ul style="list-style-type: none"> • Take 5-20 mg of Levitra one hour before you are ready to engage in sexual activity • Levitra works best on an empty stomach. Do not take Levitra after a high-fat meal • Levitra works best 30 minutes to four hours after taking the pill |
| Cialis | <ul style="list-style-type: none"> • Take 5-20 mg of Cialis at least 2 hours before you are ready to engage in sexual activity • Cialis can be taken after meals |
| Stendra | <ul style="list-style-type: none"> • Take 50-200 mg of Stendra one half hour before you are ready to engage in sexual activity • Stendra works best on an empty stomach. Do not take Stendra after a high-fat meal • Stendra works best 30 minutes to four hours after taking the pill |
| For all of these medications, if you do not achieve an erection after 6 attempts with stimulation, consider speaking to your provider about adjusting the dose or trying a different treatment | |
| Side effects for all oral medications listed above | <ul style="list-style-type: none"> • Most common side effects include headache, facial flushing and upset stomach • A small number of patients taking Viagra or Levitra may complain of a “blue cast” to their vision, sensitivity to light or blurred vision • Back pain and joint aches may occur with Cialis |
| Things to remember for all oral medications listed above | <ul style="list-style-type: none"> • Do not use Viagra, Cialis, Levitra, or Stendra more than once per day • Do not use Viagra, Cialis, Levitra, or Stendra if you take medications such as nitroglycerin, Nitrostat, Nitro-Bid, Nitro-Dur, Isordil and Ismo, or Deponit • Talk to your provider about using Viagra, Cialis, Levitra, or Stendra if you are taking Flomax, Hytrin, Cardura, Rapaflo, or Uroxatral; using these medications in combination may rarely lead to significant drops in blood pressure |

Penile Rehabilitation

Many experts have suggested that maximizing blood flow to the penis after nerve-sparing radical prostatectomy can improve erectile function and decrease the need for long-term treatment for ED after surgery. This is typically accomplished by administering regular doses of medications like Viagra, Levitra, Stendra, or Cialis without necessarily planning to have sex. In some cases physical exercises and/or a vacuum erection device may also be used.

It is important to recognize that after review of all available data on penile rehabilitation, the American Urological Association Guideline Panel on Erectile Dysfunction recommended that all patients be informed that penile rehabilitation has NOT been convincingly associated with recovery of spontaneous, unassisted penile erections. The decision of whether or not to take medications as part of penile rehabilitation should be made with consideration of the costs and potential short-term side effects.

Regardless of their use in rehabilitation, erection medications can be very helpful in helping patients achieve erection for sexual activity after prostate cancer treatment. We also encourage patients to maintain intimacy with their sexual partner during the recovery process; the emotional rehabilitation and maintenance is as important as the physical recovery.

There are numerous protocols for “penile rehabilitation.” One UCSF protocol is detailed below. Please note that this protocol has not been shown to be superior to any other and data suggesting that this will reliably help with recovery do not exist. Therefore, this protocol should be taken as a suggestion, not a necessity, in ED recovery:

Table III Penile Rehabilitation

| | |
|--|--|
| Two weeks prior to prostatectomy | <ul style="list-style-type: none"> 100mg Viagra or 20 mg Levitra 2x/week and 50mg Viagra or 10mg Levitra on days not taking 100mg Viagra/20 mg Levitra dose |
| After catheter removal | <ul style="list-style-type: none"> Viagra 50mg or Levitra 10 mg daily or Cialis 10mg 3x/week. Take in the evening to enhance nocturnal erections. Take Viagra 100mg, Levitra 20mg, or Cialis 20 mg at least weekly with sexual stimulation |
| Evaluation of sexual function 8-12 weeks after surgery | <ul style="list-style-type: none"> If you have a response to oral medications (penile fullness or erection), continue Viagra 50mg or Levitra 10 mg daily 4–5 days/ week and 100mg Viagra or 20 mg Levitra 2–3x per week. Alternatively, use Cialis 20mg 3x/week If no or marginal response to oral medications, begin penile injections and/or vacuum erection instruction. Consider beginning injections 2–3 times per week or vacuum erection use 2–3 times per week. Continue 50mg Viagra or 10 mg Levitra 10mg 4–5 days per week on days when not using injections |
| Evaluation of sexual function 12 months after surgery | <ul style="list-style-type: none"> If no spontaneous erections after 1 year and unsatisfied with penile injections or vacuum erection device, consider alternative interventions for erectile dysfunction. For patients with acquired penile curvature (Peyronie’s disease) or complex sexual concerns earlier intervention may be warranted |

NOTE: These recommendations are typical and may vary from what your provider may be prescribing. Please speak to your provider before beginning or changing any treatment.

Data from: Padma-Nathan H, McCullough AR, Levine LA, et al.: Randomized, double-blind, placebo-controlled study of postoperative nightly sildenafil citrate for the prevention of erectile dysfunction after bilateral nerve-sparing radical prostatectomy. *Int J Impot Res* 2008, 20:479–486.

Montorsi F, Brock G, Lee J, et al.: Effect of nightly versus on-demand vardenafil on recovery of erectile function in men following bilateral nerve-sparing radical prostatectomy. *Eur Urol* 2008, 54:924–931.

Mulhall JP. The role and structure of a post radical prostatectomy penile rehabilitation program. *Curr Urol Rep.* 2009 May;10(3):219-25.

Urethral Suppository - MUSE

The medicated urethral system for erection (MUSE™) system consists of a pellet of a medication called Prostaglandin E1 (PgE1, also known as Alprostadil™) which is placed inside the penile urethra. The pellets are dosed at 125, 250, 500, and 1000 mcg of PgE1. It is typical to start with low doses and adjust upwards depending on efficacy and side effects.

MUSE™ may be used when oral pills are not an option or have failed. Large studies from Europe and the United States demonstrated that MUSE™ was effective (after dose adjustment) in 43 percent of patients with ED from various causes. The major advantage of MUSE™ therapy is that it is applied locally and has few systemic side effects. However, MUSE™ may cause significant penile pain and may be transferred to a partner, leading to pain or discomfort for them during sex. It is strongly contraindicated in patients whose partners are pregnant as the main ingredient may induce uterine contractions. In rare cases, MUSE™ may also lead to bleeding, dizziness, or decreased blood pressure.

In cases where MUSE™ is effective but painful, some patients may benefit by applying a small dose of lidocaine jelly to the urethra before placing the pellet. Patients interested in MUSE™ therapy should be instructed on proper technique in their provider's office; a test dose may be applied in this setting so that side effects can be monitored.

Table IV: MUSE™ Therapy

| | |
|--------------------------|--|
| How to Use MUSE™ Therapy | <ul style="list-style-type: none"> • Patients/partners should be trained in the office • Pellet of medication is inserted into urethral opening after urination; after insertion patients are encouraged to massage their penis between two hands to dissolve the pellet • Medication is absorbed to produce erection |
| Possible Side Effects | <ul style="list-style-type: none"> • Penile pain • Can rarely cause priapism – a prolonged erection lasting greater than four hours • Fainting, dizziness, low blood pressure |
| Things to Remember | <ul style="list-style-type: none"> • After placement, stimulation is required to increase blood flow to the penis • Medication should be refrigerated • Maximum use is limited to one suppository per day |

Pellet inside urethra

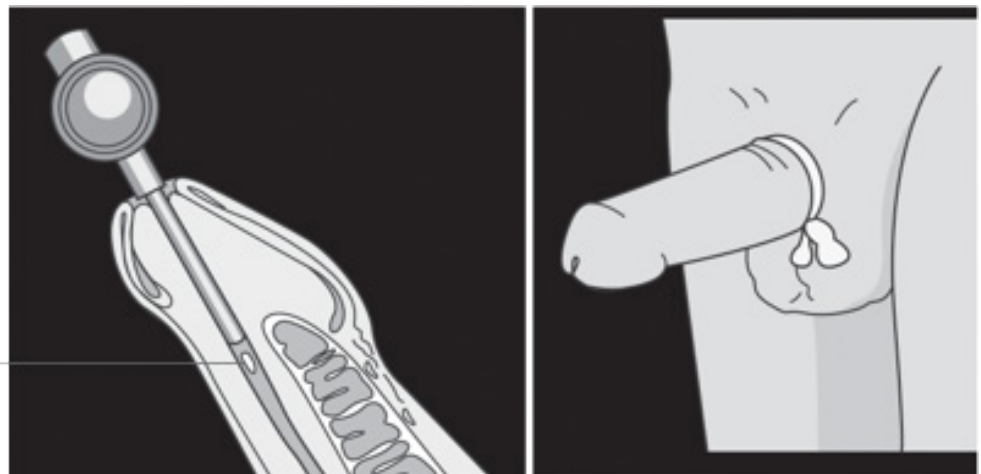


Figure 3: Application of intra-urethral suppository and constriction device. Application for intra-urethral delivery of Alprostadil. Depressing the end releases the pellet into the urethra. In some cases, application of a constriction ring may enhance penile response.

Penile Injection

When oral medication fails, penile injections to induce erection are another potential treatment for ED. While many patients object to the notion of an injection into the penis, the needle typically used for these injections is very thin and short and most patients are not bothered by it. The most commonly used agents include prostaglandin E1 or a combination of different drugs that cause increased blood flow (e.g., papaverine, phentolamine). Combinations of different medicines (aka bimix or trimix) may be more effective than single drugs alone and may also carry lower risks for side effects.

Patients must have appropriate training and education before beginning penile injection therapy. The goal of the injection medication is to achieve an erection that is sustained for sexual intercourse, but not prolonged or painful. The injections must be given in proper amounts with the appropriate technique to minimize the risk of scarring in the penis or priapism, a prolonged and painful erection which may cause permanent damage.

The medication is injected into the side of the penis into the corpora cavernosa, the paired erectile bodies of the penile shaft. After choosing the proper site to inject, the skin should be cleaned with an alcohol pad. The needle is inserted perpendicular to the penile shaft so as to enter the right spot; it is important that the medicine be administered to the inside of the corporal body, not just underneath the skin. After the medication is injected, the needle is withdrawn, and firm pressure is applied to the site to reduce the risk of bleeding or bruising; patients who take aspirin or other blood thinner should hold pressure for a bit longer. Some experts recommend that patients stand for at least 10 minutes after injection to enhance penile blood flow. Penile stimulation may also help enhance response.

Patients who are interested in injections but unable to administer the shot themselves may enlist the help of their partner. Alternatively, an auto-injector is a spring-loaded device that inserts the needle into the penis very quickly, minimizing psychological "hesitancy." A variety of injectors are available; talk to your provider if you think that an auto-injector might help you but be aware that for some patients, the "harpoon" feeling of the auto-injector hurts more than self-administered injection.

Improper injection and any subsequent scarring may hypothetically lead to penile curvature and nodules in the penis. It is important to get the proper training before beginning injection therapy. Most patients and their partners find that injection therapy is easy to perform and are very pleased with the results.

Table V: Penile Injections

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|--|--|
| <p>How to Perform Penile Injection</p> | <ul style="list-style-type: none"> • Patients should be trained in the office where possible; if not, careful counseling and review of vetted video training materials may suffice • Generally performed with insulin syringe and small needle • Skin and injection site prepared with alcohol swab • Medication is drawn up in sterile manner with insulin syringe • Medication is injected on one side of the penis • Pressure is held on injection site for several minutes • For more detail on just where and how to inject and other information on injection therapy, see Successful Self Penile Injection at https://urology.ucsf.edu/prostate-cancer-education-documents or the instruction video by Dr. Stacey Elliot Understanding Penile Injection - YouTube |
| <p>Side Effects</p> | <ul style="list-style-type: none"> • Occasionally associated with fainting, dizziness, low blood pressure • Priapism or prolonged erection (greater than 4 hours) may occur • Can cause pain, infection, bruising and scarring if patients are not trained properly |
| <p>Things to Remember</p> | <ul style="list-style-type: none"> • May require self-stimulation to increase blood flow to the penis • If erection persists for more than four hours, seek medical care at local emergency room or with your urologist • May be ineffective if patients have vascular disease or blood flow problems |



Figure 4: Intra-cavernous injection therapy. After cleaning with an alcohol swab, insert needle into side of penis and inject medication.

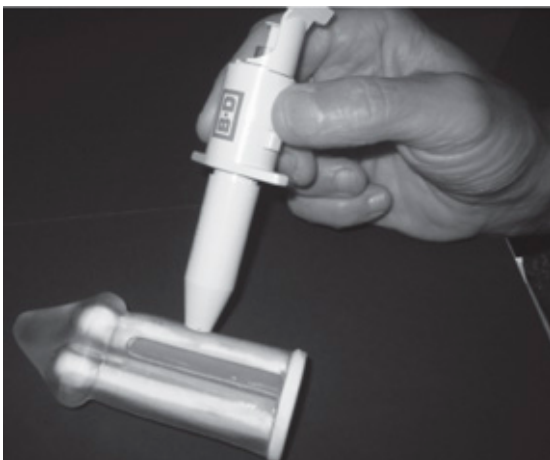


Figure 5: Auto-injection technique. The medication is drawn into the auto-injector. The side of the penis is cleaned with an alcohol swab and the injector placed against the penis. Pressing a button then activates the injector and the needle is automatically inserted.

Vacuum Erection Device

In patients who only have partial erections or those who do not respond to or want to use other treatments, a vacuum erection device may be helpful. The device consists of a plastic cylinder connected to a pump and a constriction ring. A vacuum pump uses either manual or battery power to create suction around the penis and bring blood into it; a constriction device is then released around the base of the penis to keep blood in the penis and maintain the erection. A vacuum erection device can be used safely for up to 30 minutes, which is when the constriction device should be removed. The advantage of such a device is it is relatively inexpensive, easy to use and avoids drug interactions and side effects. Side effects may include temporary penile numbness, trapping semen within the penis due to the ring, and some bruising. Some patients also report that the erection they obtain with the device feels somewhat artificial.

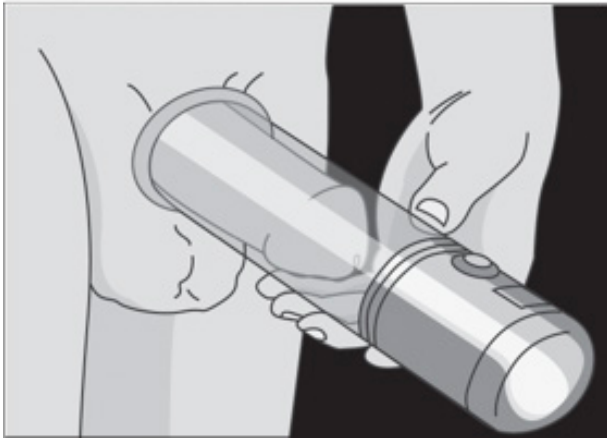


Figure 6: Vacuum Erection Device



Figure 7: Example of a three - piece inflatable penile prosthesis

Penile prosthesis

For patients with erectile dysfunction who have failed or cannot tolerate other treatments, a penile prosthesis offers an effective, but more invasive alternative. Prostheses come in either a semi-rigid form or as an inflatable device. Most patients in the US prefer the placement of the inflatable penile prosthesis as this permits a more natural appearance in the flaccid (non-erect) position.

The placement of the prosthesis within the penis is a surgery that typically requires the use of a general anesthetic. A skin incision is made either at the junction of the penis and scrotum, or just above the penis, depending on which prosthesis and technique is used. The spongy tissue of the penis is exposed and dilated; the prosthesis is then sized, and the proper device is then placed inside the erectile tissue.

The inflatable device – a pump that contains the inflation and deflation mechanism – is placed in the scrotum. The patient can control his erection at will by pushing using the hydraulic pump to inflate and a release button to deflate the device. As the nerves that control penile sensation are not injured, penile sensation and the ability to have an orgasm are typically maintained after placement.

Patient and partner satisfaction rates are as high as 85 percent for patients with carefully selected and counseled penile prosthesis placement. Full penile length might not be restored to the patient's natural erect status. Rare side effects include infection, pain and device malfunction or failure.

Causes of ED

ED can be due to psychogenic, neurogenic, vascular, hormonal, and/or medication-induced causes. Many medical conditions have been associated with ED. (See Table I)

Table VI: Causes of ED

| Category of ED | Conditions associated with ED |
|-------------------------------------|---|
| Psychological | <ul style="list-style-type: none"> • Depression/Anxiety • Schizophrenia • Performance anxiety • Stress • Relationship problems |
| Neurogenic | <ul style="list-style-type: none"> • Stroke • Pelvic surgery, injury or radiation • Spinal cord injury • Diabetic neuropathy |
| Vascular | <ul style="list-style-type: none"> • Atherosclerosis • Smoking • Hypertension • Diabetes • Trauma • Pelvic surgery, injury or radiation • Peyronie's disease |
| Hormonal | <ul style="list-style-type: none"> • Hypogonadism (low testosterone) • Hyperprolactinemia (high prolactin) |
| Drug Induced | <ul style="list-style-type: none"> • Excessive alcohol consumption • Androgen deprivation (LHRH agonists, i.e. Lupron, Zoladex) • Anti-hypertensives • Anti-depressants |
| Other Conditions Associated with ED | <ul style="list-style-type: none"> • Older age • Diabetes • Chronic renal failure • Obesity • Peripheral vascular disease • Heart disease |

Aging and Diseases Causing ED

Aging causes a progressive decline in sexual function even in healthy patients. Medical studies have discovered that as people age, there is a decrease in turgidity, or “stiffness,” of erections as well as a decrease in the force and volume of ejaculation. Also, with normal aging, there is an increase in the length of time a person requires to have another erection after experiencing orgasm, called the refractory period. Furthermore, the sensitivity to touch decreases over time as do serum testosterone levels, with an associated decrease in desire.

While it is not possible to reverse aging and the things go with it, there is no age at which a person is “too old” for sex. Those who remain physically active, eat a prudent diet, avoid obesity and tobacco use, and generally do things that are “good for the heart” can expect to at least delay the most severe manifestations of age-associated sexual dysfunction.

Psychological Causes of ED

Common causes of psychogenic ED include depression and performance anxiety. Depression is associated with decreased energy, interest and decreased libido or desire. Performance anxiety, work stress or strained personal relationships can affect erectile function in both conscious and subconscious ways.

Neurogenic ED

Penile erection depends on an intact nervous system, which means that any injury to the nervous system involved in erections can cause ED. Diseases such as Parkinson’s disease, Alzheimer’s disease, stroke or head injury can lead to ED by affecting the libido, or by preventing the initiation of the nerve impulses responsible for erections. Patients with spinal cord injuries will have decreased erections related to the extent of the injury. Patients who have undergone pelvic surgery such as radical prostatectomy, cystectomy or colectomy may have injury to the cavernous nerves that control erection. Long-standing diabetes may affect some nerves as well, which may cause ED.

Hormonal Causes of ED

Diseases and conditions that decrease circulating testosterone in the body, such as castration or hormonal therapy used to treat prostate cancer, will decrease libido and may make natural erections more difficult.

Vascular Causes of ED

Diseases such as high blood pressure, high LDL (“bad”) cholesterol, low HDL (“good”) cholesterol, heart problems, cigarette smoking, diabetes mellitus, and treatments such as pelvic irradiation to treat prostate, bladder and rectal cancers, may damage blood vessels to the penis over time. Patients with Peyronie’s disease (scarring with curvature of the penis), trauma, diabetes, and/or old age may experience damage to the spongy tissue of the penis, causing the veins to be more “leaky,” which can lead to ED.

Drugs and ED

Certain anti-depressants or anti-psychotics have been associated with ED, especially those drugs that regulate serotonin, noradrenaline and dopamine. Examples include Prozac, Zoloft and Paxil. Beta-blockers and thiazide agents used to treat hypertension are also associated with ED.

Cimetidine, a drug to treat acid reflux disease; chronic alcoholism; estrogens and drugs with anti-androgen action such as ketoconazole, and spironolactone can cause ED, decreased libido and breast enlargement. Many drugs of abuse are also associated with ED. (See Table VII)

Health Conditions associated with ED

ED is very common in patients with diabetes, liver cirrhosis, chronic renal failure, and many other chronic medical issues.

Table VII: Drugs Associated with ED

| Class of Drug | Drug |
|----------------------|--|
| Antihypertensive | <ul style="list-style-type: none"> • Clonidine • Reserpine • Beta-blockers (atenolol, propranolol, metoprolol) • Verapamil • Guanethidine |
| Anti-androgens | <ul style="list-style-type: none"> • Ketoconazole • Cyproterone acetate • Estrogen • Flutamide • Finasteride • Gonadotropin releasing hormone agonists (Lupron, Zoladex) |
| Cardiac Drugs | <ul style="list-style-type: none"> • Digoxin • Gemfibrozil • Clofibrate |
| Diuretics | <ul style="list-style-type: none"> • Thiazides (Hydrochlorothiazide) • Spironolactone |
| H2 antagonists | <ul style="list-style-type: none"> • Cimetidine • Ranitidine |
| Antidepressants | <ul style="list-style-type: none"> • Tricyclic (migraine) • Serotonin Reuptake Inhibitors (Prozac, Zoloft, Paxil) • Phenothiazines • Benzodiazepines (Valium, Xanax) • Meprobamate • Barbiturates • Lithium |
| Other Drugs | <ul style="list-style-type: none"> • Narcotics • Baclofen • Nonsteroidal anti- inflammatory drugs • Tobacco • Alcohol • Marijuana |

Summary: Mechanisms of Penile Erection

The cavernous nerves travel from the underside of the penis to the prostate. These nerves regulate blood flow within the penis during erection and flaccidity. In the flaccid state, inflow through the arteries is minimal and there is free outflow via the small veins exiting the spongy tissue just under the thick tunica (thick membrane surrounding the spongy tissue). During erection, the smooth muscle in the penis relaxes while the arteries widen to pump in more blood that expands the three cavities of the penis – also called sinusoidal spaces – to lengthen and enlarge the penis. The expansion of these cylinders compresses the small veins and reduces the outflow of blood.

(Lue, T.F., Erectile Dysfunction. New England Journal of Medicine. June 15,2000. 1802-1813.) Reprinted with Permission from the Massachusetts Medical Society

The processes of penile erection are driven by the action of nerves and blood vessels. Hormones such as testosterone also play an important role. Finally, a patient's psychological state and the health of the sexual relationship between patient and partner are critical determinants of sexual response. Patients who have stress, anxiety, and depression tend to have high levels of activation in their sympathetic nervous system; this is a natural response to any form of stress. However, that stress tends to restrict blood flow into the penis and can make erections difficult or impossible to obtain. Careful attention to both mental and physical health is important in preserving erectile function.

Further Explanation

A normal erection requires the penis' nerves and blood vessel systems to be intact. Nerves that travel to the penis include fibers from the autonomic nervous system – the part of the nervous system that functions independent of our conscious thought – and the somatic nervous system – the nervous system responsible for sensation and contraction of muscles attached to the penis.

- 1) The autonomic nervous system controls the smooth muscle in the penile blood vessels, prostate and urinary sphincters that is important for initiating penile erection and facilitating ejaculation. The autonomic nervous system includes two parts. The sympathetic division tends to restrict penile blood flow but is important for closing the bladder neck to prevent urine leakage during sex. The parasympathetic division increases penile blood flow and stimulates penile erection. Coordination of these two components of the autonomic nervous system is critical for sexual response.
- 2) Sensory nerves travel to the glans (head) and shaft of the penis; these nerves are responsible for conveying sensations such as touch, temperature, and pain to the brain and may be important for stimulating sexual responses.
- 3) Motor nerves control contraction of the ischiocavernosus and bulbocavernosus muscles that are necessary to produce a fully rigid erection and to eject semen during ejaculation. (Figure 8)

With sexual stimulation, parasympathetic cavernous nerves release chemicals (primarily nitric oxide) that significantly increase blood flow to the penis. The erectile tissue of the penis rapidly fills with blood and expands, becoming firm and erect. With increasing sexual arousal, the somatic nervous system causes the bulbocavernosus and ischiocavernosus muscles of the penis to contract, forcing additional blood into the penis and making it very rigid. At peak sexual arousal, the sympathetic nervous system causes contraction of the prostate and seminal vesicles, leading to emission, which is deposition of seminal fluid into the urethra. The sympathetic nervous system also makes the bladder sphincter close, preventing the semen from leaking into the bladder. As the amount of fluid builds in the urethra, pressure increases and the sensation of the inevitability of ejaculation is experienced. The bulbocavernosus muscle, which is under control of the somatic nervous system, then contracts and expels the semen forcibly from the urethra. Orgasm normally coincides with ejaculation.

Detumescence, or loss of erection, occurs shortly thereafter as the nerves stimulating penile erection cease releasing the molecular signals that trigger erection.

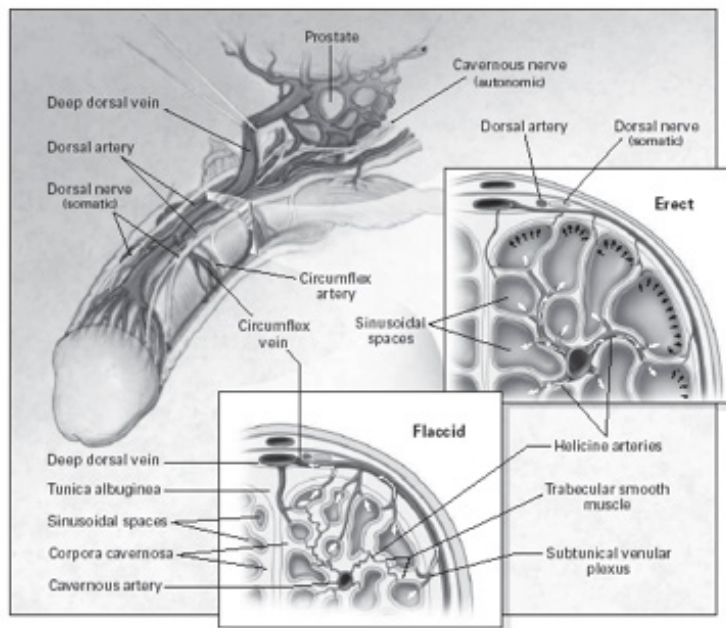


Figure 8: Mechanism of Erection

Future Directions

Innovative research over the past several years has resulted in significant strides and improvement in understanding the anatomy and physiology of sexual function. For instance, increasing knowledge about details of the cavernous nerves in the pelvis led to refinement of nerve-sparing prostatectomy. Understanding the biochemistry of normal sexual functioning led to the development of medications including Sildenafil, Cialis, Stendra and Levitra.

Current research is focused on further understanding of the specific physiologic pathways responsible for normal sexual function, developing new, more effective agents for managing ED and understanding how cavernous nerves heal and what factors can hasten the healing process.

A particularly intriguing line of inquiry over the past 10 years has been the application of low intensity shock waves (LiSW) to the penis. This counter-intuitive approach to treat ED with energy transfer is based on a growing body of evidence suggesting that shock waves may help stimulate new blood vessel growth, reduce scarring, and/or activate resident stem cells that may help restore tissues. These shock waves are similar to the shockwaves that have been used for decades in the management of urologic stones, the difference being that the energy associated with these waves is markedly less.

A number of small, randomized, placebo-controlled have demonstrated erectile function benefit to patients treated with shock waves to the penis. Unfortunately, the bulk of studies to date have had very limited follow up, with most studies reporting out results at a mean of one month. Longer term follow-up and data collection are topics of active inquiry, but do not currently exist.

Unfortunately, data on the use of LiSW in the post-prostate cancer population is scant and the degree of erection improvement in existing studies is generally mild albeit clinically significant; at this time there is no data to suggest that LiSW will be effective as a single treatment modality for the majority of patients with severe ED related to prostate cancer treatment. LiSW may eventually have a role as part of a multi-modal treatment protocol but at this time it should be considered experimental.

The AUA Erectile Dysfunction Guideline Panel recommends that LiSW only be used in the context of a clinical trial with approval from an appropriate Institutional Review Board and minimal costs to patients. It is also important to note that LiSW is distinct from acoustic wave therapy, another form of energy transfer that involves lower intensity energy transfer administered in a “sine wave” fashion as opposed to the rapid transfer associated with true shock waves. Acoustic wave therapy at this time has no evidence of any benefit at all in management of ED.

A long-standing interest in gene therapy and stem cell therapy for restoration of erectile function has not resulted in any meaningful or clinically approved therapies for ED. Despite some promising results from animal studies and a scattering of non-randomized case series, neither gene therapy nor stem cell therapy should be considered a standard of care in management of ED. The AUA Erectile Dysfunction Guideline Panel recommends that gene and stem cell therapy for ED only be used in the context of a clinical trial with approval from an appropriate Institutional Review Board and minimal costs to patients

Platelet Rich Plasma (PRP) is a therapy that is touted to have numerous benefits for ED despite a complete absence of any robust evidence from well-designed studies. The AUA Erectile Dysfunction Guideline Panel recommends that PRP for ED only be used in the context of a clinical trial with approval from an appropriate Institutional Review Board and minimal costs to patients.

Additional Resources

Books

Saving Your Sex Life, A Guide for Men with Prostate Cancer by John Mulhall 2010

Going the Distance: Finding and Keeping Lifelong Love by Lonnie Barbach and David K. Geisinger, Plume, 1993
Wonderful and realistic book about maintaining intimacy.

Hold Me Tight, Seven Conversations For a Lifetime of Love by Sue Johnson, NY, 2008
Stellar book on couples communication and intimacy.

Intimacy and ED: The Couple's Guide To Better Sex After Prostate Disease by Ralph Alterowitz and Barbara Alterowitz, De Capo Lifelong Books, 2004
Written in an honest compassionate style by a patient with prostate cancer and his wife. Discusses ED in non-medical terms with information about commercial treatments. Gives practical advice about making love. Includes everything from getting into the mood to common sense suggestions for having sexual satisfaction and intimacy when erections are not possible.

The Lovin' Ain't Over: The Couple's Guide to Better Sex after Prostate Disease by Ralph and Barbara Alterowitz. Health Education Literary Publisher, Westbury, NY, 1999

Man Cancer Sex by Anne Katz, Hygeia Media, 2010

Men, Women, and Prostate Cancer: A Medical and Psychological Guide for Women and the Men They Love by Barbara Rubin Wainrib, Michael Droller, Jack Maguire, and Sandra Haber, New Harbinger Publications, Inc., Oakland, CA, 2000

Websites

urology.ucsf.edu/patient-care/cancer/prostate-cancer

Erectile Dysfunction: AUA Guideline (auajournals.org)

www.prostatecancerfoundation.org

The Prostate Cancer Foundation funds high impact research to find better treatments and a cure for prostate cancer.

www.ustoo.org

Us TOO International Prostate Cancer Education and Support Network.

www.menshealthnetwork.org

Men's Health Network (MHN) is a non-profit educational organization comprised of physicians, researchers, public health workers, individuals, and other health professionals.

Other Sources

American Association for Marriage and Family Therapy 112 South Alfred Street, Alexandria, VA 22314-3061; Phone: (703) 838-9808; Fax: (703) 838-9805

American Association of Sex Educators, Counselors, and Therapists P.O. Box 5488, Richmond, VA 23220-0488; Phone: (804) 752-0026; www.aasect.org

American Cancer Society Phone: (800) 227-2345; www.cancer.org

CancerCare, Inc. Phone: (800) 813-HOPE, (213) 712-8400; www.cancercare.org

<https://www.urologyhealth.org>

The official foundation of the American Urological Association

Managing ED Your Health Matters Questionnaire

Please take a few minutes to answer the following questions. Your answers will help improve future editions of this guide.

Please check the appropriate box:

| Statement | Strongly Agree | Agree | Neither agree nor disagree | Disagree | Strongly disagree |
|--|--------------------------|--------------------------|-----------------------------------|--------------------------|--------------------------|
| Overall, the guide was helpful | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| The information was presented clearly and in a way that was easy to understand | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

| Statement | Too much | Just right | Too little |
|--|--------------------------|--------------------------|--------------------------|
| The amount of information presented was: | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

What was most helpful about the Guidelines?

What was least useful about the Guidelines? Why?

Should anything have been made more understandable?

Should anything be added, or discussed in more detail?

Was anything in conflict with what you already know about erectile dysfunction?

If you would like to talk about the Managing ED Guide with a member of the group that prepared it, please write your name and phone number at the bottom of the questionnaire and one of the authors will contact you.

You can e-mail your comments to urologyresearch@UCSF.edu or mail them to Your Health Matters Box 1695, UCSF Department of Urology, San Francisco, CA 94143-1695

