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Research Article

Erectile dysfunction: an update

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Abstract

Erectile dysfunction (ED) or impotence is the terminology that is used for the inability to achieve or maintain an erection sufficient for satisfactory coital activity. ED is common in every country in the world and affects many millions of males in the world. The five-question International Index of Erectile Function enables rapid clinical assessment of ED. ED can be caused by vascular, neurologic, psychological, and hormonal factors. Common conditions related to ED include diabetes mellitus, hypertension, hyperlipidaemia, obesity, testosterone deficiency, and prostate cancer treatment. Performance anxiety and relationship issues are common psychological causes. Medications and substance use can cause or exacerbate ED; antidepressants and tobacco usage are the most common. ED is associated with the development of an increased risk of cardiovascular disease, particularly in men with metabolic syndrome. Tobacco cessation, regular exercise, weight loss, and improved control of diabetes mellitus, hypertension, and hyperlipidaemia are recommended initial lifestyle interventions. Oral phosphodiesterase-5 inhibitors are the first-line treatments for ED. Second-line treatments include alprostadil and vacuum devices. Surgically implanted penile prostheses are an option when other treatments have been ineffective. Counselling is recommended for men with psychogenic ED. Treatment of ED entails working as a team with inclusion of many different clinicians and involving the ED patient as well as the coital partner of the ED patient. With careful treatment which has been tailored towards the needs of each individual ED patient with involvement of the coital partner enables the clinician and the medical care team to treat the ED patient utilising an appropriate treatment option for the patient as well educating the ED patient about all approaches to reduce as well as effective treat and prevent future recurrence. The ensuing article has detailed out overview of ED as well as miscellaneous narrations and discussions from some case reports, case series, studies related to ED.

Keywords: erectile dysfunction; impotence; history taking; examination; diagnosis; education

Introduction

Erectile dysfunction (ED) or failure to maintain an erection, or impotence had been defined as the inability to achieve or maintain an erection sufficient for sexual performance, and this has been iterated to have drastically changed more than half of a decade ago. [1] [2] It was previously assumed that erectile dysfunction is a problem primarily rooted within the psyche; however, ED is now understood to be frequently associated with a physiological basis. [1] [3] It has been iterated that organic-sources, including: vascular-, neurological- and hormonal abnormalities, with occasional psychogenic overlay, had tended often to be the causes attributed to ED in older men, while men who are under the age of 40 years had often been considered to have only psychogenic factors contributing to their ED. Nevertheless, many cases of ED quite often had tended to have organic origin, including: vascular causes, neurogenic causes, hormonal causes, causes related to side effects of medicaments. In addition, back injury and tumours within the spine or irritation or pressure on nerves within the back and spinal region could be causes of erectile dysfunction. The clinician who is assessing an individual with erectile function needs to have a high-index of suspicion related the ED and should undertake a thorough clinical assessment ensuing obtaining of a detailed history, and should undertake a thorough laboratory test assessments as well as radiology-imaging should also undertake a good clinical examination before making a diagnosis and discussing the treatment options of the individual who is afflicted by ED. The ensuing article on ED is divided into two parts: (A) Overview, and (B) Miscellaneous narrations and discussions from some case reports, case series, and studies related to erectile dysfunction.

Aim

To provide an update on erectile dysfunction

Methods

Internet databases were searched including: Google; Google Scholar; Yahoo; and PUBMED. The search words that were used included: Erectile Erection; Failure of erection, impotence; and poor erection. One hundred and ninety-six (196) references were identified which were used to write the article which has been divided into two parts: (A) Overview, and (B) miscellaneous narrations from some case reports, case series and studies related to erectile dysfunction.

Result

[a] overview

Definition and general iterations

- Erectile dysfunction (ED), or impotence, or poor erection, or no erection is a prevalent and multifaceted condition which does predominantly afflict males who are older than 40 years by age, with its prevalence iterated to be escalating within the entire world. [4]
- ED is iterated to be typified by the consistent or recurrent inability to attain and maintain an erection that is sufficient to enable the undertaking of satisfactory coital activity.
- It has been iterated that the aetiology of ED is diverse, and that ED encompasses organic, psychogenic, and mixed factors, which often had tended to be interwoven with comorbid conditions some of which include the ensuing: diabetes mellitus, cardiovascular disease, and neurological conditions.
- The complexity surrounding ED is iterated to underscore the significance of discerning the root causes of the particular case of Ed in order to provide guidance to the afflicted individual regarding the appropriate management options. [4]
- The psychological and emotional ramifications of ED could tend to be profound, effects on not only the afflicted individuals but also their partners as well as their relatives.
- If ED is not addressed by the clinician and the supporting team, it might exacerbate or induce anxiety, depression, diminished self-esteem, as well as strained inter-personal relationships. In view of this, the undertaking of a comprehensive assessment as well as appropriate and effective every patient who has been afflicted by ED would be of great and necessitating importance.
- The good thing for the clinician is that a large number of treatment options are available to be utilised by the clinician and the supporting team.
- Some of the available treatment options for ED include the ensuing: administration of oral phosphodiesterase type 5 inhibitors, hormone replacement therapies, and external vacuum devices, application of urethral suppositories, intra-cavernosal injections, topical gels, and sex therapy as well as surgical treatment may be required for very few patients including the decompression or release of nerve compression surgical procedures.
- The role that is played by the interprofessional team in managing patients with ED is pivotal. It is therefore important for the ED lead management team ensure the ensuing management plans are undertaken:
    - The ED management team needs to utilise evidence-based treatment options for erectile dysfunction, including the administration of oral phosphodiesterase type 5 inhibitors, hormone replacement treatments, and other treatment options as might be required based upon the cause of each individuals ED.
    - To undertake a comprehensive assessment of each ED afflicted individual, including obtaining of a comprehensive medical, surgical, trauma, self-medication as well as psychosocial history, in order to ascertain the aetiological factors that are contributing to erectile dysfunction of each individual.
    - To distinguish between organic and psychogenic causes of erectile dysfunction so as to guide each ED afflicted individual about the appropriate diagnostic and treatment approaches to use.
    - To involve the multi-disciplinary team (MDT) care and discussion in the provision of interdisciplinary care when managing erectile dysfunction (ED) patients including: urologists, psychologists, and sexual health specialists in order to optimize the outcomes and well-being of each ED afflicted patient.
- Erectile dysfunction (ED), which was previous referred to as impotence, has been defined as the failure to achieve or maintain a rigid penile erection that is good enough to enable satisfactory coital activity. Even though no specific time is part of this definition, some practitioners had indicated that the ED condition needs to have persisted for six months. It has been pointed out that ED is a common condition in men who are 40 years and older, and that the prevalence of ED does tend increase with the advancing of age and other co-morbid conditions. [2] [4]
- It has been iterated that ED could be a manifestation of a wide range of underlying pathology conditions and is ED is an essential but under-utilized or underrecognized cause cardiovascular risk factor. [4] [6] [7] [8] [9]
- It has been explained that any disease process, which affects the penile arteries, nerves, hormone levels, smooth muscle tissue, corporal endothelium, or tunica albuginea could emanate in the development of erectile dysfunction [ED].
- It has been iterated that ED, is closely related to cardiovascular disease, diabetes mellitus, hyperlipidaemia, as well as hypertension, among other disorders, as well as it has been stated that endothelial dysfunction appears to be another common pathway in patients with ED. [4] [11]
- It has been explained that while the vast majority of patients who are afflicted by ED would tend to have organic disease, some ED afflicted individuals might have a primary psychological problem, which would tend to be more common in younger men. [4]
- It has been pointed out that even when the underlying cause of the ED is organic, there has almost always been psychological emanations to ED regarding marital and relationship issues, cultural norms and expectations, loss of self-esteem, shame, anxiety, and depression, among others. [4]
- It has been iterated that ED could cause considerable emotional damage to the patient and their partner, as well as have a significant impact upon their quality of life; nevertheless, ED is known to be almost always a treatable condition. [4]

Aetiology

The ensuing summations had been made regarding the aetiology of erectile dysfunction: [4]

- The cause of ED has often tended to be multi-factorial. [4] It is therefore important to differentiate or ascertain whether the ED condition has an underlying psychological cause or an organic aetiology. [4]
- Depression, performance anxiety, and other sexual disorders could be strong contributing factors of ED even when organic causes also exist. [4]

- Aging is an essential factor that contributes to as well as exacerbates ED.
- As patients get older, cardiovascular diseases, hypertension, and other co-morbidities do play an increasingly significant role in ED. [4]
- Diabetes mellitus and metabolic syndrome could affect many organ systems, emanating in the accelerated deterioration of erectile function, and could disrupt the mechanisms underpinning erections on a molecular level. [4] [11] [12]
- For further explanation, it has been iterated that other causes of ED do include the ensuing conditions: [4]
    - Neurological diseases (such as multiple sclerosis).
    - Hormonal causes (hypogonadism, thyroid).
    - Trauma (for example, pelvic fractures, spinal cord injuries).
    - Hyperlipidaemia.
    - Stroke.
    - Sleep apnoea.
    - Chronic obstructive pulmonary disease, (COPD).
    - Glaucoma.
    - Multiple sclerosis.
    - Sequela of priapism.
    - Depression.
    - Prostatic hyperplasia with lower urinary symptoms (BPH with LUTS).
    - Iatrogenic causes including: post transurethral resection of the prostate gland, and a variety of medicaments including antidepressants, antihypertensives, antipsychotics, opioids, and recreational medications). [4] [13] [14] [15] [16] [17] [18] [19] as well as omeprazole. [1] [13] 14] [15] [16] [17] [18] [19] [20]

Cardiovascular Disease and Erectile Dysfunction

Summations of the association between cardiovascular disease and erectile dysfunction had been iterated as follows: [4]

- Cardiovascular disease is a very significant risk factor for ED.
- It has been documented that almost 50% of men who have known coronary artery disease that had been proven by cardiac catheterization do have significant ED. [4] [21]
- Part of the reason for the aforementioned iteration is that the coronary arteries and the penile cavernosal arteries are similar in size and they tend to develop atherosclerotic problems in a similar manner. [4]
- Since the cavernosal arteries are small, they could develop blockages from atherosclerotic plaques earlier, emanating in the development of vasculogenic ED years preceding the clinical manifestation of coronary artery disease. [4]
- Both cardiovascular disease and ED do involve endothelial cell dysfunction in their pathophysiology. [4] [21] [22]
- It has been iterated that patients would often demonstrate sub-clinical atherosclerosis long before any manifestation of overt ED develops by as much as 10 years. [4]
- The cavernosal arteries being of smaller diameter means that vasculogenic ED does often tend to precede coronary artery disease, myocardial infarctions, and strokes by up to 5 years. [4] [6] [23]
- Younger men who manifest with unexplained ED do appear to have a very significant increase, up to 50-fold, of their cardiovascular risk in their subsequent life in comparison with to an age-matched control group. [7] [24]
- In view of this clinicians do need to inform patients who have ED that ED is a significant indicator of underlying heart disease and they should refer them for further cardiovascular risk screening and treatment. [4] [6] [7] [8] [9] [10] [24]
- It has been iterated that the Prostate Cancer Prevention Trial database had shown that having ED had increased a patient's cardiovascular risk roughly equivalent to the risk of smoking or having a family history of myocardial infarctions. [1] [25] A meta-analysis of 14 studies that totalled over 90,000 men with ED had ascertained that these patients had 44% more cardiovascular events, 62% more myocardial infarctions, 39% more strokes, and a 25% increased risk of death compared to patients who had manifested without ED. [4] [26]
- It has been pointed out that ED has useful independent predictive value for the development of future cardiovascular events; therefore, the clinician needs to screen all patients with ED for cardiovascular risks. [4] [23]
- It has also been iterated that if the cardiovascular risk is adjudged to be intermediate, the clinician would then need to undertake non-invasive testing for subclinical atherosclerosis and an exercise stress test, but if the patient has a high risk, the clinician should recommend a formal cardiology referral. [4] [7] [27] [28] [29]

Besides cardiovascular disease, there are strong correlations between ED, hypertension, hyperlipidaemia, diabetes, hypogonadism, obesity, smoking, alcoholism, benign prostatic hyperplasia (BPH) with lower urinary symptoms (LUTS), depression, and premature ejaculation.

- About 40% of men with ED will have hypertension, while 35% of all hypertensive men will also have ED. [30] [31] [32]
- Hyperlipidaemia is in about 42% of men with ED.
- Undiagnosed diabetes is up to 3 times as likely in men with erectile dysfunction (28%) compared to non-diabetic men with normal erections (10%). [4] [30] [33] [34]
- Among men over 50 years of age, people with diabetes are roughly twice as likely to have ED (46%) compared to those without (24%). [4] [35]
- The longer a patient has diabetes and the more severe the disease state, the greater the risk of ED. [4] [35]
- One-third of diabetes mellitus afflicted men would have hypogonadism, which may partly explain the high correlation between diabetes and ED. [4] [36]

- Up to 35% of all men with ED would also have hypogonadism, and about 6% will have abnormal thyroid function. [4] [37] [38] While testosterone deficiency can negatively impact erectile function, vascular disease and diabetes mellitus are far more likely causes of ED. [4] [39]
- It had been pointed out that obesity is associated with a 50% increase in ED, when compared to men of normal weight. [4] [40]
- It has also been stated that one-third of the obese men with ED who enrolled in a weight loss program had resolution of their ED symptoms within 2 years. [4] [41]
- It had been reported that in smokers who had quitted smoking, their erectile quality improved by 25% after one year. [4] [42]
- It has been iterated that heavy alcohol users also report an increased risk of ED compared to the general population. [4] [33] The precise cause is said to be not certain but it has been conjectured to be due to direct alcoholic toxicity to the corporal endothelium, loss of corporal smooth muscle tissue, and early neuropathy. [4] [43]
- It has been documented that there is a strong correlation between BPH with LUTS and ED, and that the majority of men who have symptomatic BPH, as well as that up to 72%, will also have ED. [4][44] [45] [46]
- It has been iterated that patients who have depression are almost 40% more likely to have ED than men without depression. Conversely, the incidence of depression in men with ED was iterated to be almost 3 times greater. [4] [47]
- It had been iterated that obesity and morbid obesity are significant risk factors for the development of ED, and that treatment of obesity with bariatric surgery could significantly improve sexual performance.[4] [48] [49] [50]
- It has been pointed out that at least 30%, and up to 60%, of patients who have ED would also have premature ejaculation. [4] [30] [51]
- It had also been iterated that successful treatment of the ED would often alleviate premature ejaculation in view of reduced performance anxiety, as well as that ED treatment usually alleviates premature ejaculation. [4]
- It has been pointed out that prescription medications are considered to cause one-quarter of all cases of ED, as well as that of the 12 most commonly prescribed medications in the United States of America (USA) 8, listed erectile dysfunction as a possible side effect. [4] [37] [52] These drugs do include the ensuing: most antidepressants (especially selective serotonin reuptake inhibitors), cimetidine, ketoconazole, spironolactone, sympathetic blockers (methyldopa, clonidine, and guanethidine), thiazide diuretics, and other antihypertensives. (Angiotensin-converting enzyme [ACE] inhibitors and calcium channel blockers are the least likely to cause ED.) Beta-blockers are only a minor contributor to ED, while alpha-blockers improve erectile function. [4] [53] [54]
- It has been iterated that out of the prostate cancer patients who undergo radical prostatectomy surgery, 85% could expect ED post-operatively, compared to an ED rate of only 25% for men who received definitive radiotherapy, [4] [55] [56] as well as that this data refers to patients who did not have ED preceding their prostate cancer treatment. It has also been stated that utilisation of robotic surgery for radical prostatectomies has not changed the post-operative incidence of ED. [4]
- It has been pointed out that the role of bicycle riding in ED is controversial. [4]
- It has also been iterated that traditional racing bicycle seats place considerable pressure directly upon the perineal nerves as well as the pudendal and cavernosal arteries, which indicates it could be a potential problem for cyclists. [4] [57] [58]
- It has been iterated that a 2020 meta-analysis of 3330 cyclists compared to 1524 non-cycling controls had indicated a significantly increased risk of ED in cyclists. [4] [59

Epidemiology

The ensuing summations had been iterated regarding the epidemiology of ED. [4]

- Many patients do fail to seek medical attention, and many physicians tend to be reluctant to ask patients regarding their sexual health; and hence, obtaining accurate values for the true prevalence of ED has tended to be difficult. [4]
- It has been iterated that the best available data had indicated that 52% of men within the US, who are between 40 and 70 years of age do have erectile dysfunction. [4] [5] [33] [60]
- It has also been stated that, it is estimated that at least 30 million to 50 million men within the US and at least 150 million men globally have ED. [4] [61] [62]
- It has also been iterated that the aforementioned values are likely a gross underestimation of the actual number of men with ED due to reporting bias, cultural factors, a general failure by many physicians to inquire about their male patient's sexual health and embarrassment issues. [4] [60]
- The prevalence of ED has been iterated to be closely related to age and the presence of other co-morbid conditions such as diabetes mellitus, hypogonadism, as well as cardiovascular disease. [4] [60]
- It has been iterated that the best available data from the Massachusetts Male Aging Study had suggested an overall prevalence of 52%, with the incidence increasing with age. [4] [33]
- It has also been stated that at the age of 40 years, about 40% of men are affected by ED, while 70% would report having ED by the age of 70 years. [4] [33]
- It has been documented that The National Health and Social Life Survey and similar studies had confirmed the aforementioned findings. [4] [63] [64]
- It has been iterated that estimates had indicated that erectile dysfunction would afflict 322 million men worldwide by the year 2025. [4] [62]

Pathophysiology

The ensuing summations had been made regarding the pathophysiology of erectile of erectile dysfunction: [4]

- The critical process in penile erection activity is the relaxation of the intracavernosal smooth muscle, [65] and this process is

iterated to permit increased blood flow into the corpora cavernosa, which fills with blood and compresses the emissary veins, reducing venous outflow. [4] [65]

- The para-ventricular and medial preoptic nuclei of the hypothalamus had been stated to control this process. [4] [65]
- It has furthermore, been iterated that signals traverse through the parasympathetic nervous system to the parasympathetic nerves of the S2-S4 sacral plexus and then to the penis through the cavernosal nerves. [4]
- It has also been iterated that Nitric oxide released by the cavernous nerve terminals initiates the erectile process, while nitric oxide from endothelial cells acts to maintain it. [4] [65]
- It has in addition been iterated that Nitric oxide stimulates the production of cyclic guanosine monophosphate (GMP) when it enters the smooth muscle. [4] [66]
- It has been pointed out that Cyclic GMP activates protein kinase G, which then opens potassium channels and closes calcium channels, and that low intracellular calcium causes the intracavernosal smooth muscle tissue to relax, increasing arterial flow with simultaneous veno-occlusive activity. [4] [65] This is stated to emanate into a rigid erection with minimal blood flow into or out of the corpora once the erection is established. [4]
- It has been iterated that when penile phosphodiesterase degrades cyclic GMP, the corporal smooth muscle contracts again, and the process reverses. [4] [65]
- It has been pointed out that pathology that arises from any of the aforementioned processes could emanate in the development of the erectile dysfunction. [4] [65] [67]

The clinicians undertaking of history taking and clinical examination

The ensuing summations had been made regarding the clinicians undertaking of history taking and clinical examination. [4]

- Prior to embarking upon any treatment or further investigations, clinicians need to undertake a thorough medical and history taking, including detailed sexual history, and clinical examination. [4]
- It is also necessary to obtain a complete medication list, including supplements, mainly if targeting prostate problems, as they often contain anti-androgens. [4] [68]
- Clinician should not forget to ask about details of the individuals self- medication drugs. [4]
- Some authors had found it helpful to give the patient a scoring system so they could better communicate the degree of their erectile rigidity, with 100% being the best and hardest they ever had, 0% being flaccid, and 50% being just barely hard enough for penetration. [4] The authors iterated that this simple scoring system had made it much easier for patients to indicate how rigid their erections are and track their progress pursuant to their treatment, [4] and alternatively, a questionnaire, such as the International Index of Erectile Function Questionnaire (IIEF), could be given to the patient to fill out privately. [4] It has been pointed out that the questionnaire had been validated and found to be helpful for the monitoring of the severity of erectile dysfunction and treatment efficacy. [4] [69]

The author(s) had recommended that typical sexual history questions should include the ensuing details: [4]

- How hard or rigid an erection can you now get (with 50% being just barely enough for penetration)?
- What is the best or most rigid erection you can get right now?
- How long can that erection last?
- Does the penis feel numb or in any way unusual?
- Does the penis lose rigidity during foreplay?
- Does the penis lose rigidity only when attempting vaginal penetration?
- Does the penis stay erect and rigid until immediately after penetration? (This could be from anxiety or a venous leak.)
- Do you still get morning erections?
    - If so, are the morning erections any better or longer-lasting than the erections you get when having intercourse?
    - If not, when was the last time you had a good morning erection?
- Any overnight erections? If so, how hard are they?
- Does the hardness of the erection vary much from one day to the next?
- Has there been any time or recent circumstance when the erection worked any better, such as with masturbation or an alternate partner?
- How is erectile rigidity with masturbation compared to when attempting intercourse?
- When was the last time your erections worked normally and you had sexual intercourse?
- When did the erection trouble begin?
- Did it start suddenly or gradually? (sudden, unexplained onset of ED is almost always psychogenic)
- Was there any significant change in your life that happened at about the same time as the erection trouble started? New relationships or medications?
- Is the main problem insufficient rigidity or maintenance?
- Is the problem stable or getting worse?
- Is there any history of a particularly traumatic sexual event in your past?
- What do you use for contraception?
- Have you already tried any treatments? If so, what?
- Are ejaculation and orgasm normal even if the erections are not?
- How hard does the erection get at ejaculation?
- Do you feel your general interest in sexual activity is roughly normal?
- If ED was not an issue, how often would you desire to have sexual intercourse?
- Does your partner agree with that frequency?

- Does your partner know you are here seeking treatment? If so, are they encouraging?
- Would your partner be willing to become involved in treatment?
- How often do you and your partner currently attempt intercourse?
- Which of you usually initiates sexual activity and how?
- If not successfully treated, what will happen to your relationship?
- Are the erections straight or curved?
- Is there a problem with libido, interest, ejaculation, or orgasm? If so, when did these other symptoms start?
- Would you be satisfied if we could get the erections up to 65% or 75%, and they would last for 10 or 15 minutes? If not, what would you consider a successful treatment?

It has been advised that other helpful things that need to be elicited in the patient history taking include: vascular risk factors (for example, hypertension and diabetes mellitus), lifestyle factors (such as smoking, activity level, alcohol intake, as well as utilization of any recreational medicaments), and general medication history. [4] [70] It has been advised that pursuant to obtaining of the patient's permission, the partner should also be present for the history taking as they could provide a different perspective upon the relationship; their views would help measure the response to the treatment. Having the coital partner involved in the treatment process could greatly improve upon the outcome. [4] The partner of the patient might provide a different perspective upon the nature of sexual dysfunction as well as relationship issues that are not otherwise forthcoming directly from the patient. [4] The ensuing further iterations and recommendations had been made: [4]

- Clinicians should complete a general cardiovascular examination, as erectile dysfunction could be the first symptom of an underlying vascular or cardiac disease. [4] [68]
- Clinicians should check the peripheral pulses of their patients and they should measure the blood pressure of their patients.
- The genitalia should be carefully inspected by the clinician, looking at the testicular size for hypogonadism, signs of infection such as redness and discharge in acute balanoposthitis, the presence of penile fibrosis or plaques as in Francois de la Peyronie disease, and phimosis due to the inability to retract the foreskin. [4] Hair distribution, breast size looking for features of gynecomastia, and the undertaking of a detailed neurological examination would be helpful. [4]
- Clinicians had been advised to evaluate the cremasteric reflex by gently scratching or stroking the upper inner thigh while observing the scrotum as well as it had also been iterated that a normal reflex would be a retraction or elevation of the ipsilateral testicle. [4] [68] It has been iterated that this reflex activates if the thoracolumbar erection centre is intact. [4] [68]
- It has been pointed out that erectile dysfunction could be the first manifestation of otherwise silent cardiac or vascular disease, so a full cardiovascular workup should be completed by the clinician in all patients without an apparent cause of their ED. [4] [24] [68] [71]

Evaluation

The ensuing summations had been made regarding the evaluation of individuals who manifest with erectile dysfunction: [4]

- Many clinicians often find it challenging and uncomfortable to initiate discussions about their patient's sexual health, a sentiment that is rooted in cultural norms and the potential for embarrassment. [4] [72]
- In view of this the ensuing phraseology would be very acceptable when vocalized to patients in a way that indicates, by intonation, that the questioner is expecting that everything would be fine and normal. If you ask, "How is your sex life? Everything working OK for you?" men without any sexual problems or issues are likely to respond with a quick "everything is fine" response. If the patient hesitates with their response or indicates that things are "not like they used to be," this should indicate that there is a potential sexual disorder that warrants further inquiries and investigation. [4]

Psychogenic ED and Mental Health

The ensuing summations had been made about psychogenic ED and Mental Health: [4]

- It is beneficial to differentiate between obvious psychological and organic causes of ED as well as to verify that the patient has erectile dysfunction and not another type of sexual disorder, such as premature ejaculation. [4]
- Careful questioning should be able to ascertain if the patient has actual, organic erectile rigidity failure or some other sexual problem. [4] [73]
- Items in the history which point towards a psychological aetiology include sudden onset of erectile dysfunction (primarily if related to a new partner or a major life-changing event), situational ED, normal erections with masturbation or a different partner, the presence of good morning erections and high daily variability in erectile rigidity. [4] [73]
- Clinicians should refer obvious cases of psychogenic ED to an appropriate mental health professional. [4] [68]
- Even without obvious psychological issues, the involvement of mental health experts could help deal with associated problems, such as reducing performance anxiety, promoting treatment adherence, improving relationship issues, identifying interpersonal conflicts, and setting realistic expectations for the couple. [4] [68] [74] [75]

It has been iterated that recommendations for a mental health evaluation could be complex and uncomfortable for a clinician, especially during a patient's initial visit. [4] Some of the strategies to clarify and support the need for a mental health consultation, making it more readily accepted by patients, had been summated to include the ensuing:

- A mental health assessment should be just part of their routine evaluation; and they would recommend it for everyone with ED. [4]
- It should just be a one-time evaluation, an opinion. If the clinician does not find any problems, the clinicians should cross that off their list and move on. [4]
- The assessment is like a blood test; if everything is normal, the clinicians then go on, and if not, they deal with it. [4]
- Clinicians should take vital signs including blood pressure and temperature, at every office visit for the same reason because

problems in these areas would not always be obvious, yet if not diagnosed and treated, they could cause severe harm to the ED afflicted individuals. [4]

- Identifying any emotional, anxiety, or relationship issues earlier would mean they could be dealt with properly, and if clinicians find nothing, they proceed. [4]
- Most patients with ED would not have an underlying psychological cause, but just having ED would damage relationships, increase stress, diminish self-esteem, and create anxiety, all of which interfere with a successful outcome. [4]

Blood Testing

Summations that had been made regarding blood testing of ED afflicted individuals includes the ensuing: [4]

- There are no specific blood tests that are required for the initial evaluation of ED. Nevertheless, many clinicians would order routine blood testing to include a complete blood count (CBC) and electrolytes, baseline renal and liver function tests, HgbA1c to screen for diabetes mellitus, and a lipid profile.
- Checking a morning serum testosterone level was recommended by the 2018 AUA Guidelines on Erectile Dysfunction. Nevertheless, some experts feel it is not necessary unless there are other symptoms indicative of hypogonadism, such as loss of sexual desire or testicular atrophy on clinical examination. [4] [68]
- If not measured initially, clinicians are advised to check morning serum testosterone levels to exclude hypogonadism if patients fail oral PDE-5 ED treatment [4] [68]
- Other blood tests that may be requested by clinicians include: LH and prolactin, if hypogonadism is present, and sickle cell testing should be undertaken in patients of African/Caribbean descent. [4]
- Clinicians need to measure thyroid function (TSH) test and serum prostate-specific antigen in appropriate patients, which is optional. [4]
- Clinicians should refer patients with abnormal laboratory test results to their primary healthcare providers for further evaluation and treatment. [4]
- A standard laboratory workup might include CBC, a comprehensive metabolic panel (CMP, which includes liver and renal function), a lipid profile, TSH level, HgbA1c, and a morning testosterone assay on all new patients that present for evaluation of their ED. [4]

Shared Decision Making

The ensuing summations had been made regarding shared decision making in the assessment and management of erectile dysfunction afflicted individuals include the ensuing: [4]

- According to the 2018 AUA Guidelines Statement on ED, the recommended approach to patients with ED involves shared decision-making. [4]
- In this approach, the clinician does inform and does educate the patient and his partner using the best available evidence about the various appropriate treatment options available to them; further diagnostic testing might be reasonable or advisable. [4] [68] [76]
- A frank discussion by the clinician about the pros and cons of testing and treatment ultimately leads to an informed patient choice which corresponds to the couple's values and preferences. [4] [77]
- This is stated to be similar to the older "goal-oriented" approach of famed urologist Dr. Tom Lue, who urged healthcare professionals to focus upon realistically discussing the treatment options with patients to facilitate their personal treatment selection rather than pursuing extensive testing, which ultimately does not significantly affect outcomes.
- It has been iterated that the basis for this approach is that, with the possible exception of psychotherapy for purely psychogenic ED, there is no effective cure; identification of the underlying cause is only helpful in detecting other potential health issues and comorbidities. [4]
- It has been stated that given this fact, the focus changes from expensive diagnostic testing that would not significantly affect the outcome to facilitating patient treatment selection after a detailed discussion on reasonable therapeutic options. With this in mind, no other investigations are generally necessary for patients with ED, even though specialized testing might be helpful in selected individuals. [4] [68]

Further Testing Which is Optional

It has been iterated that all of the ensuing tests for patients with ED should be considered as optional for selected patients only: [4]

[A] Penile biothesiometry

- Biothesiometry of the penis is stated to involve a straightforward office screening test for penile neuropathy using skin vibrational threshold sensitivity. [4] The process entails placing a blunt-tipped vibrating probe upon the right and left shaft, as well as upon the glans penis. [4]
- Patients are required to indicate when they first sense the tip vibrating, determining their threshold vibrational sensitivity. [4] This value is then compared to age-based normal standards after obtaining 5 separate readings at each site and averaging the results. [4] [78]
- It has been iterated that while penile biothesiometry does not directly examine erectile nerves, it is a reasonable, safe, and cost-effective office test for penile neuropathy.
- Patients who test positive for biothesiometry may undergo more specialized nerve testing. [4] [78] [79] [80]
- While not confirmed, some had suggested that individuals with an abnormal biothesiometry test might display hypersensitivity to intracavernosal injection therapy due to denervation hypersensitivity. [4]

Nocturnal tumescence testing (NPT)

- It has been stated that nocturnal tumescence testing (NPT) proves valuable in differentiating psychogenic erectile dysfunction from organic erectile dysfunction.
- Testing entails measuring the frequency, tumescence (circumference changes), duration, and maximal rigidity of nocturnal erections.
- Nocturnal erections require complete functioning of the neurovascular axis and typically occur during REM sleep.

- An average functioning man has between 3 erections and 6 erections a night, with a mean duration greater than 30 minutes, maximal rigidity greater than 70% at both base and tip, as well as an increase in circumference of over 3 cm at the base and 2 cm at the tip. [81]
- This process is then repeated, usually for 3 nights.
- Men who have purely psychogenic ED would typically demonstrate normal NPT tracings, while those with organic problems will show abnormal nocturnal erectile activity.
- Hypogonadism would often cause a decrease in rigidity while maintaining some tumescence in NPT studies. [82] [83]
- Today, NPT monitoring is rarely undertaken or considered necessary to differentiate psychogenic from organic erectile dysfunction reliably.
- A careful and detailed personal and sexual history typically enables the determination of significant psychogenic factors. [73]

Penile duplex Doppler ultrasound scan

- It has been pointed out that penile duplex Doppler ultrasound scan does measure arterial vascular flow and checks for cavernous veno-occlusive dysfunction (venous leak). [4] [84]
- It has been stated that this test might also be helpful after penile trauma, post-priapism, Francois Gigot dela Peyronie's disease, and in patients with ED who fail to respond to oral agents. [4] [84]
- The ultrasound scan finding in ED is typically done by giving the patient an intra-cavernosa injection of a vasoactive drug, usually 20 µg of prostaglandin E1. (This also serves as a clinical trial of penile injection therapy.) Following the injection, the peak systolic velocities (PSV) are then measured. A normal value is > 35 cm/s, while a reading of < 25 cm/s suggests arterial insufficiency. The value of < 25 cm/s was found to have 100% sensitivity and 95% specificity for patients with abnormal pudendal arteriography. [4] [85]
- Hypertensive patients who have vasculogenic ED, as demonstrated by a significantly reduced cavernosa-arterial flow on duplex ultrasound scan, should be referred for a complete cardiac evaluation in view of their increased cardiovascular risk. [4]
- It has been stated that ultrasound scan can also demonstrate cavernous veno-occlusive dysfunction, which is often called "venous leak" by patients; this finding represents the failure of penile corporal rigidity despite adequate arterial inflow. Venous leak becomes evident when rapid detumescence occurs despite normal peak systolic and end-diastolic velocities (EDV > 5 cm/s). [4] [86]
- Measuring the vascular resistive index (RI) could aid in the diagnosis of veno-occlusive dysfunction. Calculation of RI is undertaken using the formula: RI = (PSV-EDV)/PSV. An RI < 0.75 is consistent with veno-occlusive dysfunction. [4] [87] The main benefits of this investigation are its non-invasiveness and its ability to exclude both penile arterial and venous dysfunctions accurately. Nevertheless, the results are very user-dependent, and abnormal anatomy could give rise to erroneous readings. Furthermore, the information provided would remain the same treatment for most patients. [4]
- It has been advised that clinicians need to refer hypertensive patients who have vasculogenic ED and demonstrate significantly reduced cavernosal arterial flow on duplex ultrasound for a complete cardiac evaluation. [4]

Dynamic infusion cavernosometry and **cavernosography**

- It has been recommended that dynamic infusion cavernosometry and cavernosography should be undertaken for patients in whom a site-specific venous leak is suspected--usually for patients who have suffered pelvic/perineal trauma or those who have primary erectile dysfunction (for example, if the-individual had never been able to achieve an erection). [4]
- These tests are stated to usually precede corrective vascular surgery. [4] [88] [89]
- Two needles are placed into the penis to infuse saline simultaneously and measure intra-cavernous pressure. The inability to raise intra-cavernous pressure to match the mean systolic blood pressure with the saline infusion or the sudden fall in intra-cavernous pressure after stopping the saline infusion demonstrates veno-occlusive dysfunction. [4] [88] [89]
- It has been explained that cavernosography shows the site of the veno-occlusive dysfunction. [4] [90]

Pudendal arteriography

- It has been iterated that pudendal arteriogram provides a clear visualization of the penile arterial vasculature and that this test is reserved for young patients who have erectile dysfunction resulting from trauma in cases where revascularization surgery is a potential consideration. [4] [91]
- The anatomy of the internal iliac, internal pudendal, and penile arteries, are carefully studied in pudendal arteriography. [4] [91]
- The inferior epigastric arteries are also examined for potential use in penile revascularization during the undertaking of pudendal arteriography. [4] [91]

Endothelial cell dysfunction

- It has been iterated that endothelial cell function could be tested by various means, such as the penile nitric oxide release test, peripheral arterial tonometry, and flow-mediated dilation. [4]
- It has been pointed out that there are also different serum markers such as C reactive protein, endothelin 1, vascular cell adhesion molecule-1, as well as the presence of endothelial progenitor cells and microparticles. [4] [92]
- It has been iterated that none of these tests for endothelial cell function has much current clinical utility, and they are of research interest only at present. [4]

Treatment / Management

It has been iterated that the initial treatment of ED entails improving the general health status through lifestyle modifications. This treatment not only improves upon erectile function but it reduces cardiovascular risk. It had been advised that the recommended lifestyle modifications should include the following: [4]

- Increased physical activity
- Switching to a Mediterranean diet or nutritional counselling
- Cessation of smoking, drugs, and alcohol

- Gaining reasonable control of diabetes mellitus, lipids, and cholesterol

It has been recommended that clinicians should carefully review the patient's drug history in order to remove or alter the doses of offending medications. It has also been advised that clinicians should offer men who have a psychological cause psychosexual counselling. It has also been iterated that with the patient's consent, this counselling should be offered to the partner as well. [4]

L-arginine

- It has been iterated that L-arginine is an amino acid supplement which is the essential substrate for producing nitric oxide synthase, the enzyme that produces nitric oxide in the body. [4]
- Supplemental L-arginine increases nitric oxide synthase levels, theoretically improving erection function. [4]
- It has been iterated that many studies had shown some efficacy in treating mild to moderate ED with L-arginine supplementation (1500 mg to 5000 mg). [4] [93]

Eroxon

- It has been iterated that eroxon is a proprietary topical gel and the only OTC product which has an FDA recommendation for treating ED. [4]
- The gel contains carbomer, ethanol, glycerine, propylene glycol, and potassium hydroxide. [4]
- After the application of the gel to the glans penis, which takes about 15 seconds, the gel quickly evaporates and provides an immediate cooling effect upon the glans. This rapid cooling stimulates the nerves and induces tissue warming, resulting in the relaxation of smooth muscles. Consequently, this process enhances blood flow to the corpora and relaxes intra-cavernosa smooth muscles, promoting erectile function and rigidity. [4]
- It has been iterated that the gel has successfully treated ED in about 60% of men, typically within just 10 minutes. At 20 minutes, the success rate increased to 75%, equivalent to the reported efficacy of prescribed oral agents. This efficacy was maintained over 12 and 24 weeks in studies, with minimal side effects. Unfortunately, there are only a few studies with a limited number of individuals available on this gel. [4]
- Only one of the studies was double-blinded, and none were placebo-controlled. [4]
- It is therefore clear how this new gel might work with existing ED therapies, such as phosphodiesterase-5 inhibitors like sildenafil and tadalafil. [4]
- The gel is currently available within the UK and Belgium. When it will be available in the US is still undetermined. While the expected cost in the US is unknown, in the UK, a single application cost is equivalent to $8. [4]

Oral phosphodiesterase-5 inhibitors (PDE-5 inhibitors)

- It has been iterated that oral phosphodiesterase-5 inhibitors (PDE-5 inhibitors), such as sildenafil and tadalafil, are usually the first-line treatment of ED. [4]
- They are effective in a wide range of aetiologies, including cardiovascular disease, diabetes mellitus, hypertension, and hypogonadism. [4] [94]
- PDE-5 inhibitors act by decreasing the degradation of cyclic GMP through phosphodiesterase inhibition, which increases the relaxation of cavernosa smooth muscle and intra-cavernosa arterial blood flow.
- It is important to note that PDE-5 inhibitors do not initiate the erectile response.
- Sexual stimulation is necessary to release nitric oxide from the vascular endothelium and penile nerve endings to commence the erectile process. [4]
- PDE-5 inhibitors are highly effective and have an overall success rate of up to 76%. [4] [95]
- It has been advised that patients on sildenafil should remember to take it on an empty stomach, or it would not be absorbed. [4]
- It has been pointed that adverse events would occur in about 40% of patients but are usually mild. [4]
- The most common side effects are headache, indigestion, nasal stuffiness, and mild visual changes such as temporary light sensitivity or bluish coloration to vision. There had been rare reports of permanent blindness from non-arteritic anterior ischemic optic neuropathy with PDE-5 inhibitors. [4] [96] [97]
- It has been pointed out that there are also rare reports of unilateral deafness, typically starting within 24 hours of ingestion, related to these drugs. [4] [98] [99] [100] Fortunately, these reactions are stated to be rare, but it has been recommended that patients should be appropriately informed. [4]
- It has been iterated that different PDE-5 inhibitors have varying half-lives, which can influence the patient's final selection. [4]
- It has been advised that clinicians need to note the importance of using these drugs with antihypertensives and alpha-blockers with caution and that they should not be used at all with nitrates due to potentially dangerous, profound hypotension. [4]
- It has been advised that patients who fail PDE-5 inhibitor therapy should try at least one other PDE-5 medication, as up to 50% of initial treatment failures will respond to a different PDE-5 drug. (Clinicians need to check serum testosterone levels in patients who fail PDE-5 therapy if this was not measured earlier.), and those who are hypogonadal might benefit by the addition of testosterone supplementation to their PDE-5 inhibitor therapy. [4] [101]
- It has been iterated that: instructing patients, on how to take their medication correctly is essential. For example, sildenafil is poorly absorbed and might be ineffective if taken with food, and it also frequently requires several therapeutic tries before it begins working successfully. [4]
- It had been stated that results from studies on adding daily L-arginine supplements to sildenafil or tadalafil therapy had demonstrated a significant improvement in IEFF scores and erectile function compared to sildenafil or tadalafil monotherapy. [4] [93] [102] [103]

Testosterone supplementation

- It has been iterated that testosterone supplementation does appear to be more effective as a treatment for low libido than for ED. [4] [104] [105]

- It has been recommended that clinicians should commence with oral PDE-5 inhibitors as the initial treatment for most patients with both ED and hypogonadism. [4]
- Testosterone supplementation is reasonable in those with proven hypogonadism and ED who have already failed PDE-5 inhibitor therapy or who also have low libido. [4]
- Patients with hypogonadism with borderline erectile rigidity are most likely to benefit from testosterone supplementation. [4]
- The patients with ED who received the most significant benefit from testosterone supplementation were those with the most severe level of hypogonadism. [4] [106]
- It has been pointed out that overall, only 35% of all patients with hypogonadism with ED would demonstrate significant improvement in their erectile function from testosterone supplementation. [4] [107]
- It has been iterated that testosterone monotherapy is not considered an effective treatment for ED. [4] [68]

External vacuum devices

- It has been iterated that external vacuum devices are an excellent, non-surgical option for many patients with ED. [4]
- The outer cylinder of the device is placed over the penis and pressed to the body to create an airtight seal. The patient then utilises a small, hand-operated (or battery-powered) vacuum pump to create negative pressure around the penis, which engorges the corpora with blood. Placing an elastic band around the base of the penis maintains the artificial erection. The vacuum could then be released, leaving the artificial erection maintained for up to 30 minutes. Practice with the device does seem to improve outcomes, and manual dexterity is required. The efficacy rates of these devices had been documented to be high, at about 70% to 80%, but the patient satisfaction rates are low. [4] [108] [109]
- It has been iterated that external vacuum device therapy is a cost-effective, safe, and highly efficient long-term treatment for ED, suitable for frequent use if desired. Nevertheless, using the device initially requires practice for optimal performance. It remains a good, safe, and effective non-invasive option for patients who deem it practically acceptable. [4]

Intraurethral prostaglandin E1 (alprostadil) pellets

- It has been stated that intra-urethral prostaglandin E1 which is also called medicated urethral system for erection or MUSE, are available for use as urethral suppositories. [4]
- The patient first voids and then places the tip of the insertion device inside the urethral meatus and pushes the plunger to deposit the prostaglandin E1 pellet into the pre-moistened distal urethra, where it will dissolve with a gentle hand massage. [4]
- The medication is then absorbed via the urethra and makes its way into the corpora cavernosa, where it causes muscle relaxation, resulting in an erection. [4]
- Overall efficacy of the pellets is stated to be reportedly good, generally at about 50% to 65%. [4] [110] [111]
- Results from a large, double-blinded, placebo-controlled study of over 1500 men with chronic ED is stated to have found that two-thirds of patients had responded to intraurethral prostaglandin E1 pellet therapy sufficiently to have intercourse. [4] [111]
- It has been iterated that intraurethral prostaglandin E1 pellets are commercially available in 4 different strengths, but the 2 largest dosages are used most often are 500-1000 mcg. [4]
- Side effects of the pellets are stated to include urethral burning and somewhat variable efficacy even from the same dosage, possibly depending on the precise site of pellet application. This treatment is stated to be used relatively infrequently due to its high cost, the variability of efficacy, and the frequent need for patients to purchase at least 6 doses at a time. [4]

Intra-cavernosa Injections

- It has been stated that intra-cavernosa injections with prostaglandin E1 are frequently the next choice of treatment if oral PDE-5 inhibitors are unsuccessful. [4] [108]
- Intra-cavernosa injections of papaverine (an alpha-blocker and vasodilator) as a therapy for ED were first described in 1988 and had been documented to have delivered good results. [4] [112]
- Since then, many agents had been found which could cause smooth muscle relaxation, vasodilation, and erections when injected (alone or in combination) into the corpora cavernosa. These include papaverine, prostaglandin E1, phentolamine, and atropine. [4] [113] [114] [115]
- The single agent that is used most frequently today is stated to be prostaglandin E1, which is associated with fewer systemic adverse events and good efficacy while offering reduced priapism risk and less fibrosis compared to other agents. [4]
- This agent is iterated to work through its effects to increase cavernosa cyclic AMP, the body's most effective, natural smooth muscle relaxant and is the only FDA-approved agent for intra-cavernosa injection therapy of ED. [4] [68]
- It has been stated that a single injection, which is sufficient as the corpora cavernosa shares vascularity, is done on the side of the penile shaft near the base to avoid the urethra (ventrally) and the dorsal neurovascular bundle. [4] [116] [117]
- It has been advised that patients should switch sides to minimize scarring. Typically, patients are advised to use short, 27 to 30-gauge needles with 1 cc syringes of insulin type. [4]
- It has been iterated that intra-cavernosa injection therapy had shown high effectiveness in up to 94% of patients. [4] [118] Nevertheless, prostaglandin E1 is stated to be relatively expensive and somewhat painful when injected into the corpora. [4]
- It has been pointed out that combination therapy had become popular using a relatively standard combination of papaverine 30 mg, phentolamine 1 mg, and prostaglandin E1 20 mcg/cc (known as "TriMix") or by adding 0.2 mg of atropine to make "QuadMix." These combinations need to be prepared by a compounding pharmacy. In general, they are about twice as effective as prostaglandin E1 alone, tend to cost less, and usually avoid the discomfort associated with intra-cavernosa prostaglandin E1 injections when used alone. [4]
- It has been iterated that the dosages and concentrations could be adjusted to double strength levels if required. Only prostaglandin

E1 is recommended by the FDA for intra-cavernosa injection therapy for ED. [4] [68]

- It has been iterated that usually, the initial trial dosage is 0.2 to 0.25 cc, which increases slowly to give the patient a rigid erection for a reasonable time and no more than 90 minutes and optimally only about 45 minutes. [4] It had also been iterated that if the corpora cavernosa, are healthy with good vascularity, intra-cavernosa injections are almost always going to be successful. [4]
- It had also been iterated that failure of intra-cavernosa injection therapy is a good diagnostic indicator of vasculogenic ED. [4]
- Side effects from intra-cavernosa injections had been iterated to include: pain, priapism, bleeding or bruising at the injection site, and scarring of the tunica. [4]
- It has been pointed out that patients need to be carefully counselled not to exceed the recommended dosage for them as it is highly tempting to inject more medication "just to be sure" or because the initial effect appeared sub-optimal. [4] Clinicians had been advised to be prepared to offer a priapism antidote (usually a diluted phenylephrine solution) either in their office or in the emergency department. [4] [119]
- It has been advised that patients must be warned not to increase the injected dosage without the approval of their clinician, not to mix it with other ED agents such as PDE-5 inhibitors, and to go to the nearest emergency department for reversal therapy if their erection lasts longer than 4 hours to prevent permanent damage to the corpora. [4]

Combined therapy

- It has been iterated that with intra-cavernosa injections (or intraurethral prostaglandin pellets) plus the addition of a PDE-5 inhibitor could be very effective if neither treatment alone is successful. [4] [114] [120] [121] [122]
- It has been stated that the two treatments utilise different chemical mediators (cyclic AMP for injections, cyclic GMP for PDE-5 inhibitors), which synergistically enhances their combined activity. [4]
- It has been iterated that while effective, the risk of priapism is stated to increase, and experience with this type of combined therapy is limited. [4] [123] [124] [125] Nevertheless, it might be worth a clinical trial before considering penile prosthesis surgery or giving up entirely on those who are not surgical candidates. [4] [126]

Penile prostheses

- It has been iterated that penile prostheses are a surgically invasive treatment, which are typically offered when all other, less intrusive measures fail or are otherwise unacceptable. [4]
- These devices are surgically inserted into the corpora cavernosa to restore erectile function artificially. [4]
- There are 2 main types available: malleable and inflatable. The malleable prosthesis is physically manipulatable into a straight or bent position per the patient's wishes. The inflatable type becomes erect by activating a small pump in the scrotum, which fills the inflatable penile balloon cylinders from a hidden fluid reservoir surgically implanted in the lower abdomen. [4]
- It has been stated that older men with limited manual dexterity or mental health issues find the malleable prostheses more manageable. [4]
- In contrast, it has been stated that most men, especially from younger generations, typically prefer inflatable devices due to their more natural operation and function. [4]
- Patients with diminished pelvic or penile sensation might have better outcomes with inflatable devices to avoid painless ulcers and erosions due to excessive pressure from the malleable rods on the skin. [4]
- It has been pointed out that complications emanating from these devices include: erosion, leakage, infection, and possible mechanical failure. [4]
- It has been iterated that early inflatable penile prostheses had many problems, including: infections, penile deformities, aneurysm formation, leakage, pump failures, and other mechanical issues. [4]
- It has also been pointed out that current devices have resolved these problems and are mechanically reliable. [4] The current mechanical failure rate for inflatable prostheses is stated to be less than (<) 5% over 5 years. [4] [127] [128]
- Other improvements in the device had been stated to include antibiotic or hydrophilic coatings that further reduce the risk of infection. [4] [129] [130] [131][132] [133]
- The overall infection rate for penile prostheses is stated to be now only about 3% but might be as high as 10% in patients with prior implants, diabetes, or spinal cord injuries. [4] [134] [135]
- It has been stated that even though many patients with ED will not wish to have surgery, penile prosthesis implantation procedures tend to have very high patient satisfaction scores of about 90%. [4] [136] [137]
- It has been iterated that the long-term results are not quite as good, with only 41% of patients, indicating they are still using their penile prosthesis after 20 years. [4] [136] [138]

Penile revascularization surgery

- It has been iterated that penile revascularization surgery is undertaken only in a small sub-group of patients, with an estimated occurrence rate of 5% in all patients with ED. [4] [139]
- It has been iterated that this procedure is ideally considered for younger patients, who are younger than 30 years who develop ED following pelvic/perineal trauma who have sustained an isolated vascular injury. [4]
- It has been iterated that arterial insufficiency needs to be demonstrated on penile Doppler ultrasound scan and then identified on a formal arteriogram. [4] Clinicians had been advised to undertake the revascularization operation by anastomosing the inferior epigastric artery to the dorsal artery of the penis or directly to the corpus cavenosum. [4]
- It has been stated that the long-term results are only marginal. [4]

Arterial balloon angioplasty

- It has been stated that arterial balloon angioplasty has been undertaken successfully for focal arterial stenosis of the pudendal or penile arteries. [4] Nevertheless, improvement does

not usually last due to recoil arterial narrowing and restenosis unless using drug-eluting stents. [4]

- It has also been stated that this therapy is not yet the standard of care and is only helpful in patients with focal, identifiable arterial stenosis in vessels large enough to accept a stent. [4] [140] [141] [142]

Venous ligation surgery

- It has been iterated that venous ligation surgery which is undertaken for veno-occlusive dysfunction involves embolizing or ligating the penile veins (for example, the deep dorsal vein). [4]
- It has been iterated that this surgery is not recommended as long-term results do not show lasting efficacy. [4] [68] [140] [143]

Low-intensity shockwave therapy

- It has been iterated that low-intensity shock wave therapy has demonstrated efficacy, particularly in patients with severe ED not responding to PDE-5 inhibitors. [4] [144] [145] [146] [147] [148]
- It has been iterated that the presumed mechanism of action of low-intensity shockwave is via improved cavernosa haemodynamics, induction of endothelial cell proliferation, and activation of endogenous stem cells as well as from penile revascularization. [4]
- It has been documented that shockwave therapy increases angiogenic factors that promote neovascularization, restore smooth muscle activity, and attract stem cells. [4].
- This therapy is also documented to increase vascular endothelial growth factor, neuronal nitric oxide synthase, and other natural bioactive agents. [4] [149]
- It has been iterated that the exact mechanism of action of shockwave therapy has not been well understood, but it does seem that the effect is dose-dependent, as 3000 pulses per session give better results than 1500 or 2000 pulses. [4] [145]
- It has been pointed out that while early results of low-intensity shock-wave therapy appear to be promising in optimal candidates, some study results had demonstrated no effect. [4] [150]
- It has been iterated that meta-analysis of all the currently available studies had demonstrated that low-intensity shockwave therapy generally does provide a clinically significant short-term improvement in erection rigidity and function. [4] Nevertheless, the lack of long-term data makes it difficult to recommend at this time. [151]
- It has been stated that overall, low-intensity shockwave therapy does appear to be a reasonable, safe, and moderately effective initial treatment for relatively healthy patients with mild to moderate ED, with an overall success rate of 30 months in about 40% of patients. [4] [148] [151] [152]
- It has been iterated that negative risk factors that limited successful outcomes of low-intensity shock wave therapy include: advanced age, hypertension, smoking, obesity, hyperlipidaemia, high pre-therapy SHIM (Sexual Health Inventory for Men) scores, and lengthy duration of ED. [4]
- It has furthermore, been iterated that low-intensity shockwave therapy is relatively useless in men with severe ED. [4] [153]
- It has been pointed out that the therapy is still considered investigational within the US and has not been recommended by the FDA. [4] [68]
- It has been iterated that intra-cavernosa stem cells and platelet-rich plasma therapy are promising but experimental, requiring more investigation. [4] [68] 154] [155] [156] [157] [158] [159]

Penile rehabilitation therapy.

- It has been pointed out that many studies are looking at penile rehabilitation therapy after radical prostatectomy surgery which has indicated a benefit, but there is no consensus opinion on the exact treatment selection, duration, or timing. [4] The majority of the published studies had been stated to suggest that a combination of PDE-5 inhibitors together with external vacuum device therapy offers the best results, even though intraurethral pellet therapy and intra-cavernosa injections had been successful. [4] [160]
- It has been stated that Tadalafil offers a theoretical benefit over sildenafil based upon its longer half-life and pharmacokinetics, but there is insufficient data to make any formal recommendation. [4] [161] [162] [163] [164]
- It has been iterated that early use of penile rehabilitation treatment is recommended lasting up to 1 year after surgery, but the exact timing had not been adequately studied. [4] [161] [162] [163] [164]
- It has been documented that even though there is currently insufficient data to support any recommendation, it does seem reasonable that penile rehabilitation techniques should also help prostate cancer patients who select definitive radiotherapy. [4] [165] However, with sildenafil and tadalafil now being generic and low-cost, there seems to be little harm in recommending their early use after definitive prostate cancer treatment.

Differential Diagnoses

- It has been iterated that the primary differential diagnoses for ED would include: hypogonadism, loss of libido, depression with low mood, and other psychological conditions. [4]
- It has been stated that this condition may be the first manifestation of diabetes mellitus or cardiovascular disease, as well as depression.
- It has been iterated that differentiating between true erectile dysfunction and other sexual disorders, such as premature ejaculation, is essential and this is usually easily accomplished by obtaining a good sexual history of the patient. [4]

Prognosis

The ensuing summations had been made about the prognosis of erectile dysfunction: [4]

- The prognosis of ED is dependent on the cause. [4]
- Psychosexual causes of ED are stated to generally have a good response to counselling, and most other causes of ED respond favourably to oral PDE-5 inhibitors. [4] [166] If not, there are multiple other options for treatment, including external vacuum devices, intraurethral prostaglandin pellets, intra-cavernosa injections, and combined therapy. [4]

- It has been stated that ED patients rarely fail all of these non-surgical options and that there is still penile prosthesis implantation surgery, which remains highly successful. [4]
- Almost every patient with ED can be treated successfully with the currently available treatment options. [4]

Complications

The ensuing summations had been made about the complications of ED: [4]

- It has been iterated that complications of ED could cause a strain upon relationships and negatively impact the quality of life of these patients. [4]
- The cardiovascular pathologies and diabetic complications which may accompany ED are correlated with other health issues as well. [4]
- Priapism from PDE-5 inhibitor medications is relatively uncommon at only about 3% of all priapism cases despite the widespread utilisation of these medications. [4]
- Penile injection therapy is involved in about 8.8% of priapism cases and trazodone in about 6%, while second-generation antipsychotic drugs are stated to be responsible for 33.8%. [4] [167]
- It has been iterated that treatment for drug-induced priapism is intermittent intra-cavernosa injections of diluted phenylephrine solution, 200 μg at a time, about 5 to 10 minutes apart until detumescence or when a maximum dose of 1 mg of phenylephrine is delivered. If this fails, a surgical shunting procedure will be necessary. [4]
- It has been iterated that treatment of ED complications should commence quickly, as permanent corporal fibrosis can occur with delayed therapy. [4] [168] [169]

Deterrence and Patient Education

- It has been iterated that with regard to deterrence and patient education regarding ED, one of the most important messages to the public would be that this condition is treatable and men should seek help if they suffer from erectile dysfunction. [4]
- It has been iterated that in order to prevent ED, positive, healthy, basic lifestyle choices should be addressed such as smoking, diet, and exercise. [4] [170]
- It has been recommended that it is also paramount to aggressively treat existing medical conditions, such as diabetes mellitus, obesity, and hypertension, properly.

Pearls and Other Issues

Summations that had been made regarding pearls and other issues of erectile dysfunction include the ensuing: [4]

- Extensive and expensive diagnostic testing for ED is not warranted as there are no curable organic causes. [4]
- Basic blood tests for serum testosterone level, lipids, HgbA1c, thyroid, renal, and kidney function are reasonable, but more extensive testing is unnecessary for most patients. Instead, the focus of therapy is generally to assist the patient in selecting the optimal therapy for him and then giving it a clinical trial. Penile prosthesis surgery is usually undertaken for patients who have failed all other treatment options and are still highly motivated to have erectile function restored. [4]
- When oral PDE-5 agents do not work, clinicians are advised to make sure they are correctly taken and to check the serum testosterone level of the patient. [4]
- While mechanical and obvious, external vacuum devices are said to be reliable and work reasonably well for most patients. In one study, where 1500 ED patients were carefully taught, counselled, and followed-up, the success rate in achieving an adequate erection was an astonishing 94.5%. [4] [109]
- Yohimbine is a tree bark that had been utilised for decades as an oral therapy for ED, primarily before the advent of PDE-5 inhibitors, by having a central and peripheral effect on erectile function and blocks presynaptic alpha-adrenergic receptors, which decrease adrenergic tone while increasing cholinergic effects. [4]
- Yohimbine is stated to be safe and inexpensive, with no significant adverse events noted. [4]
- Yohimbine is stated to pose challenges as it requires 3 times daily dosing, and clinical studies did not demonstrate significant efficacy when compared to a placebo. [4] Consequently, the 2018 AUA Guidelines on Erectile Dysfunction did not include a recommendation for this therapy. [4]
- There is, however, renewed interest in utilising yohimbine in combination with PDE-5 inhibitors, but there is insufficient data to recommend it. [4] [171] [172] [173]
- Trazodone is stated to be a sedative and antidepressant which is often still used as a sleep aid. [4] [174]
- A high risk of priapism was noted in patients taking trazodone, so some practitioners began using it off-label to treat ED. [4] [175] [176] [177] While this treatment has clearly shown some good activity in treating ED, particularly in patients with psychogenic erectile dysfunction, its effectiveness when used in combination with PDE-5 inhibitors and the optimal dosage is unestablished, even though a dose of 150 to 200 mg had been suggested. [4] [178]
- It has been iterated that in a patient who has failed all other treatments short of penile prosthesis surgery, clinicians need to consider a trial of combined therapy with a full dose intra-cavernosa injection, such as 1 cc of "TriMix" or "QuadMix," together with a PDE-5 inhibitor. [4] While data is limited and the risk of priapism increases, there is a reasonable chance this would work and prevent the need for undertaking surgery. [4]
- Venous leak surgery has not been recommended in view of poor outcomes. [4]
- It has been iterated that many other ED treatments are investigational only and that such experimental treatments include: low-intensity extracorporeal shockwave therapy, intra-cavernosa stem cell installation, endovascular revascularization with angioplasty of the pudendal or penile arteries, and platelet-rich plasma therapy. [4] [140] [149] Out of these, stem cell therapy appears to be the most promising and is being actively investigated. [4] [179]
- Clinicians had been advised to warn patients about the dangers of taking dietary supplements which claim to improve sexual performance, confidence, or stamina. Many of these products,

from one-third to half, have been found to contain PDE-5 inhibitors, which can be dangerous for patients taking nitrates for cardiovascular disease. [4]

Evaluation and Treatment Summary

- Inquire about sexual health in all adult patients. Use a non-threatening, non-judgmental intonation and use phraseology such as, "How is your sex life? Is everything working OK for you?"
- Be aware that if the patient gives a qualified or hesitant answer, it probably indicates he has a sexual problem.
- The next step is a careful medical and sexual history, together with a comprehensive physical examination.
- Clues to possible psychological causes include sudden onset of ED, high erectile variability, good morning erections, and good erections with masturbation or alternate partners.
- Refer psychogenic sexual disorders to appropriate mental health providers.
- No specific testing for ED is required, but a blood panel consisting of a morning testosterone level, CBC, CMP, liver and renal function, lipid panel, HgbA1c, and TSH would not be unreasonable.
- No other tests are required or recommended for most patients with ED.
- Employ "shared decision making" by carefully discussing the pros and cons of all the various treatment options that are not contraindicated with the patient and their partner if possible.
- First-line therapy is usually with oral PDE-5 inhibitors. Make sure the patient takes them correctly.
- Try at least 2 different oral agents before moving on to another therapy. Check serum and morning testosterone levels in all patients who fail oral PDE-5 therapy.
- Intracavernosal injections are usually the subsequent treatment, but remember intraurethral suppositories and external vacuum devices.

If even 1 full cc of double strength "TriMix" or "QuadMix" injections are not working, and all other non-surgical therapies, such as external vacuum devices, have been tried unsuccessfully, consider a trial of combined therapy by asking the patient to take an oral PGE-5 inhibitor about an hour before the "Trimix" injection—before going on to penile prosthesis surgery. Tell patients to be cautious when using combined therapy of this type, as it carries a high risk of inducing priapism. This therapy is a consideration only for patients who have failed all other treatment options and are considering a penile prosthesis or just giving up. Failure of this combined therapy to work indicates severe damage to the corpora cavernosa, which may only be relieved by a penile prosthesis implant.

Enhancing Healthcare Team Outcomes

The ensuing summations had been made regarding enhancing healthcare team outcomes: [4]

- ED is stated to be managed in the community with the help of primary healthcare providers, specialist nurses, pharmacists, and psychologists. [4]
- Nevertheless, it has been advised that patients who are unresponsive to initial management should be referred to secondary services, classically urologists, for further investigations and management. [4] [68]
- It has been pointed out that prompt diagnosis and treatment of ED could reduce the emotional stress that is felt by patients and their partners. [4]
- It has been pointed out that effective management of ED demands a collaborative approach involving various healthcare professionals to optimize patient-centred care, outcomes, and safety. [4]
- It has been iterated that physicians lead by diagnosing underlying causes, devising treatment strategies, and ensuring interprofessional communication. [4]
- It has been iterated that advanced practitioners contribute by conducting assessments, discussing treatment options, and offering patient education. [4]
- It has been stated that nurses play a crucial role in patient education, providing emotional support, and monitoring treatment adherence. [4]
- It has been iterated that pharmacists ensure accurate medication selection, dosage, and potential interactions. [4]
- It has been iterated that team communication among these professionals fosters comprehensive care and minimizes medication errors. [4]
- It has been stated that care coordination involves streamlining appointments, facilitating referrals, and monitoring patient progress. [4]
- It has been iterated that the synergy of these roles ensures a holistic approach, enhances patient safety, and improves team performance, resulting in optimized outcomes for individuals with ED. [4]

[B] Miscellaneous narrations and discussions from some case reports, case series, and studies related to erectile dysfunction.

Shamloul, et al. [2] made the ensuing iterations:

- Erectile dysfunction is a common clinical entity which afflicts mainly men, who are older than 40 years of age.
- In addition to the classical causes of erectile dysfunction, such as diabetes mellitus and hypertension, many common lifestyle factors, such as obesity, limited or an absence of physical exercise, and lower urinary tract symptoms, had been linked to the development of erectile dysfunction.
- Substantial steps had been taken in the study of the association between erectile dysfunction and cardiovascular disease.
- Erectile dysfunction is a strong predictor for the development of coronary artery disease, and cardiovascular assessment of a non-cardiac patient manifesting with erectile dysfunction is now recommended.
- Substantial advances had occurred with regard to the understanding of the pathophysiology of erectile dysfunction which ultimately had led to the development of successful oral treatments, namely the phosphodiesterase type 5 inhibitors.
- Nevertheless, oral phosphodiesterase type 5 inhibitors have limitations, and present research had thus been investigating cutting-edge treatment strategies including gene and cell-based technologies with the aim of discovering a cure for erectile dysfunction.

Lue [180] made the ensuing iterations:

- Erectile dysfunction is defined as the inability to achieve and maintain an erection sufficient to permit satisfactory sexual intercourse.
- Erectile dysfunction had been estimated to affect 20 million to 30 million men in the United States, and ED may result from psychological, neurologic, hormonal, arterial, or cavernosal impairment or from a combination of these factors. .

Yafi et al. [60] made the ensuing iterations:

- Erectile dysfunction is a multidimensional but common male sexual dysfunction which entails an alteration in any of the components of the erectile response, including organic, relational and psychological.
- Roles for non-endocrine (neurogenic, vasculogenic and iatrogenic) and endocrine pathways had been postulated.
- In view of its strong association with metabolic syndrome and cardiovascular disease, cardiac assessment might be warranted in men who manifest with symptoms of erectile dysfunction.
- Minimally invasive interventions to relieve the symptoms of erectile dysfunction include: lifestyle modifications, oral drugs, injected vasodilator agents and vacuum erection devices.
- Surgical treatments are reserved for the subset of patients who have contraindications to these nonsurgical interventions, those who do experience adverse effects from (or are refractory to) medical treatment and those who also have penile fibrosis or penile vascular insufficiency.
- Erectile dysfunction could have deleterious effects upon a man's quality of life; most patients have symptoms of depression and anxiety related to sexual performance.
- These manifesting symptoms, in turn, afflict his partner's coital experience and the couple's quality of life. The Primer had highlighted many aspects of erectile dysfunction, had summarized new treatment targets and ongoing preclinical studies which evaluate new pharmacotherapies, and had covered the topic of regenerative medicine, which represents the future of sexual medicine.

Rew et al. [181] made the ensuing iterations:

- Erectile dysfunction (ED) is the inability to achieve or maintain an erection sufficient for satisfactory coital performance.
- ED is stated to be common, and does afflict at least 12 million U.S. men.
- The five-question International Index of Erectile Function allows rapid clinical assessment of ED.
- ED could be caused by vascular, neurologic, psychological, and hormonal factors.
- Common conditions related to ED include: diabetes mellitus, hypertension, hyperlipidaemia, obesity, testosterone deficiency, and prostate cancer treatment.
- Performance anxiety and relationship issues are common psychological causes.
- Medicament and substance utilisation could cause or exacerbate ED; antidepressants and tobacco use are the most common. ED is associated with an increased risk of cardiovascular disease, particularly in men with metabolic syndrome.
- Cessation of tobacco, regular exercise, weight loss, and improved control of diabetes mellitus, hypertension, and hyperlipidaemia are recommended initial lifestyle interventions.
- Oral phosphodiesterase-5 inhibitors are the first-line treatments for ED.
- Second-line treatments for ED include alprostadil and vacuum devices.
- Surgically implanted penile prostheses are stated to be an option when other treatments had been ineffective.
- Counselling is recommended for men who are afflicted by psychogenic ED.

Wessells et al. [182] made the ensuing iterations:

- Male sexual health had taken on increased importance as the United States population ages, develops coexisting medical conditions and undergoes interventions that could affect sexual function.
- They characterized the burden and severity of disease, treatment patterns and economic consequences of erectile dysfunction.

Wessells et al. [182] used analytical methods to generate these results which had been described previously. Wessells et al. [182] summated the results as follows:

- Erectile dysfunction was self-reported by almost 1 out of 5 men and it had increased with age.
- Erectile dysfunction might have been more commonly reported in Hispanic men and in those with a history of diabetes mellitus, obesity, smoking and hypertension.
- In most databases black American men had rates of use for office visits and inpatient hospital care which were twice those of other racial groups, even though these rates were not controlled for comorbid conditions or other regional and socioeconomic factors.
- Utilization of diagnostic tests markedly decreased, while pharmacological therapy, especially with oral phosphodiesterase-5 inhibitors, had markedly increased.
- Penile implant surgery had continued to be undertaken with most patients electing inflatable devices.
- Extrapolating from the population-based estimates of erectile dysfunction prevalence and current use trends had shown that the cost of treatment nationwide could reach $15 billion if all men sought treatment.

Wessells et al. [182] made the ensuing conclusions:

- The burden of disease due to erectile dysfunction within the United States would increase with the aging of the male population, increasing prevalence of comorbid conditions, expanded treatment seeking behaviour and costs of pharmaceutical therapy.
- Accurate estimates of economic cost would require better understanding of the pathogenesis, treatment seeking behaviour, patient preference for therapies, success of treatments and relative satisfaction with oral pharmacotherapy and penile implants.

Muneer et al. [5] made the ensuing summary iterations:

- Erectile dysfunction has organic and psychogenic components
- The incidence of erectile dysfunction increases with age and is a marker for endothelial dysfunction
- Changes in lifestyle can help men with erectile dysfunction and reduce cardiovascular risk factors
- First line treatment is with oral phosphodiesterase-5 inhibitors and second line treatment uses intraurethral or intracavernosal prostaglandins
- Men who do not respond to drugs have the option of penile prosthesis surgery
- Erectile dysfunction is defined as the inability to achieve and maintain a penile erection adequate for satisfactory sexual intercourse.
- Increasing public awareness and the universal availability of effective oral drugs had resulted in more men seeking treatment for the problem and an increase in the number of primary care consultations and referrals to secondary care.
- The World Health Organization had iterated that "Sexual health is fundamental to the physical and emotional health and wellbeing of individuals, couples and families, and to the social and economic development of communities and countries.
- Erectile dysfunction afflicts the quality of life for both patients and partners and is associated with relationship difficulties.

Selvin et al. [183] assessed the prevalence of erectile dysfunction and quantified the associations between putative risk factors and erectile dysfunction within the US adult male population. Selvin et al. [183] undertook a cross-sectional analysis of data from 2126 adult male participants in the 2001-2002 National Health and Nutrition Examination Survey (NHANES). Selvin et al. [183] assessed erectile dysfunction by a single question during a self-paced, computer-assisted self-interview. These data were nationally representative of the noninstitutionalized adult male population in the US. Selvin et al. [183] summated the results as follows:

- The overall prevalence of erectile dysfunction in men aged ≥20 years was 18.4% (95% confidence interval [CI], 16.2-20.7), indicating that erectile dysfunction affects 18 million men (95% CI, 16-20) in the US.
- The prevalence of erectile dysfunction was highly positively related to age but was also particularly high among men with one or more cardiovascular risk factors, men with hypertension, and men with a history of cardiovascular disease, even after age adjustment.
- Among men who had diabetes mellitus, the crude prevalence of erectile dysfunction was 51.3% (95% CI, 41.9-60.7).
- In multivariable analyses, erectile dysfunction was found to be significantly and independently associated with diabetes mellitus, lower attained education, and lack of physical activity.

Selvin et al. [183] made the ensuing conclusions:

- The high prevalence of erectile dysfunction among men with diabetes and hypertension suggests that screening for erectile dysfunction in these patients may be warranted.
- Physical activity and other measures for the prevention of cardiovascular disease and diabetes mellitus may prevent decrease in erectile function.

Rossi and Pellegrino [184] stated that two cases of impotence following a treatment with etretinate had been reported in the literature, and that Acitretin is the principal active metabolite of etretinate. Rossi and Pellegrino [184] reported a case of erectile dysfunction associated with the use of acitretin. Rossi and Pellegrino [184] reported a 39-year-old Caucasian man, who presented his incapacity to reach and maintain a penile erection during a course of acitretin for the treatment of a severe form of psoriasis. His clinical examination, laboratory findings and psychological analysis did not demonstrate any abnormalities. Two weeks pursuant to the withdrawal of acitretin, the patient had reported a normalization of his sexual activity. Rossi and Pellegrino [184] made the ensuing conclusions:

- Retinoids had been associated with male reproductive system dysfunctions in human and animal studies.
- Clinicians should be aware of the possibility of acitretin-induced erectile dysfunction.

Beach et al. [185] made the ensuing iterations:

- Over the preceding 9 years, drugs for erectile dysfunction (ED) had been increasingly prescribed for men with erectile difficulty.
- These drugs, phosphodiesterase 5 (PDE5) inhibitors, help men with ED to obtain and sustain an erection, improving both sexual function and sexual performance satisfaction.
- Nevertheless, these drugs contain side effects.

Beach et al. [185] reported a-56-year-old man, who developed an erythematous, circle-shaped lesion upon his penis. The lesion was reported to be recurrent, with evidence of desquamation. Beach et al. [185] determined the source of the recurrent lesion based upon its morphology and the patient's verbal history. Beach et al. [185] summated the results as follows:

- A clinical diagnosis of fixed drug eruption owing to utilisation of the PDE5 inhibitor tadalafil (Cialis) was made.
- He was not rechallenged with the drug.
- Nevertheless, he had experienced a subsequent recurrence of the eruption upon inadvertent rechallenge.

Beach et al. [185] made the ensuing conclusions:

- They believed their reported case was the first report of this type of reaction owing to tadalafil.
- Therefore, fixed drug eruption is a newly observable side effect of this medicament.

Badal et al. [186] stated that erectile dysfunction had been explored as a condition secondary to elevated prolactin; nevertheless, the mechanisms by which elevated prolactin levels cause erectile dysfunction had not yet been clearly established. Badal et al. [186] reported a patient who had a history of prolactinoma, who had been suffering from persistent erectile dysfunction despite testosterone supplementation and pharmacological and surgical treatment for the prolactinoma. Badal et al. [186] stated that patients who had had both prolactinaemia and erectile dysfunction had been reported in the literature, but they did not find any report of a patient with persistent erectile dysfunction in the setting of testosterone supplementation and persistent hyperprolactinemia refractory to treatment. Badal et al. [186] concluded that their reported case had provided evidence supporting the idea that suppression of erectile function occurs in both the central and peripheral nervous systems independent of the hypothalamic-pituitary-gonadal axis.

Heo et al. [187] reported a 42-year-old man who had manifested with back pain. For years preceding his manifestation, he had undergone treatment for back pain which had been caused by his falling down injury he had sustained. He had also complained about having erectile dysfunction, which was at that time considered to be of psychological origin within other departments. He was upon assessment found to have grade IV leg weakness as well as left lower thoracic para-vertebral area tenderness. He did undergo computed tomography (CT) scan of thorax, plain radiograph, as well as whole body scan, which illustrated normal findings. Pursuant to his undergoing diagnostic medial branch block within his lower thoracic vertebra, his pain had partially settled; nevertheless, his erectile dysfunction had continued. In view of the patient's symptoms, Heo et al. [187] ordered a magnetic resonance imaging (MRI) scan to be undertaken. The MRI scan which the patient underwent demonstrated an extra-medullary mass at T9 level. He then underwent neurosurgical operation for removal of the tumour, and pathology examination of the excised tumour confirmed pathology features of Schwannoma. Ensuing his operation, his symptoms had completely improved. Heo et al. [187] concluded that despite the fact that erectile dysfunctions had frequently tended to be presumed to be associated with psychological origin, they had reported a patient who had manifested with symptoms which had emanated from spinal tumour.

Hitiris et al. [188] made the ensuing iterations:

- Sexual dysfunction had been reported in both men and women with epilepsy.
- Sexual dysfunction associated factors are diverse but include, among others, antiepileptic drugs.

Hitiris et al. [188] reported the cases of 5 men who reported mild to moderate erectile dysfunction or impotence for the first time when they were treated with the new antiepileptic drug pregabalin as add-on therapy.

Androshchuk et al. [189] stated that erectile dysfunction (ED) is an early marker of coronary artery disease (CAD) and often ED manifests before the development of symptomatic CAD. Androshchuk et al. [189] reported a 60-year-old man who had ED, and who had demonstrated limited response to the standard management strategies and was subsequently treated with percutaneous pelvic intervention (PPI) of the internal pudendal artery. While on the table for PPI, the patient reported having a classical history of angina, on which basis he underwent coronary angiography and was found to have narrow proximal left anterior descending stenosis. Coronary artery stent placement was then undertaken using standard techniques. Androshchuk et al. [189] made the ensuing conclusions and declaration of learning points:

- PPI of pudendal artery stenoses with stents is feasible and can improve cavernosal blood flow and venous leakage as well as erectile function.
- Coronary artery disease is more common in patients who have erectile dysfunction (ED) than is generally appreciated, and should be considered in all patients with ED and vice versa.
- In patients with ED with limited response to standard therapies, percutaneous pelvic intervention of the erectile-related arteries is effective at restoring adequate blood flow to the penis, and can produce clinically significant improvement in objective and subjective measures of erectile function.
- Further studies confirming the efficacy and durability of this therapy are required before widespread adoption of endovascular angioplasty and stenting as a standard therapeutic option for vasculogenic ED.

Do et al. [190] made the ensuing iterations:

- HMG-CoA reductase inhibitors, which is more commonly called statins, are widely used in the pharmacological management of hyperlipidaemias.
- The most common adverse drug reactions (ADRs) of statins are muscular.
- Other reported ADRs of statins together with other lipid-lowering medications, namely fibrates, include erectile dysfunction (ED).
- The relationship between ED and exposure to statins had not clearly been established even though a number of significant case reports had associated ED with exposure to statins.

Do et al. [190] investigated the association between exposure to statins and the occurrence of ED on the French Pharmacovigilance System Database. Do et al. [190] stated that within the French Pharmacovigilance System Database, the case/ non-case method was used to measure the disproportionality of combination between a statin and ED. They also stated that the cases were defined as those reports corresponding to the ADR of interest (i.e. ED) and non-cases were all reports of ADRs other than that being studied. The study period was from 1 January 1985 to 31 December 2006, and the study was limited to males aged from 13 years to 80 years. Do et al. [190] estimated the association between ED and statins by calculating a reporting odds ratio (ROR) of exposure to each drug, with its 95% confidence interval (CI). Do et al. [190] summated the results as follows:

- Among the total of spontaneous reports selected (110 685), exposure to statins had been identified in 4471 cases (4%), of which 51 reports (1.1%) concerned ED, whereas 431 (0.4%) cases of ED were found in the 106 214 reports without exposure to statins ($p< 0.0001$).
- The mean delay of onset of ED after commencing statins, known for 19 cases, was 62 days (median 29 days).
- In 56.9% of the cases, recovery had occurred after withdrawal of statin, and rechallenge was positive in five cases.
- The association was found to be statistically significant for all statins (adjusted ROR [aROR] = 2.4; 95% CI 1.8, 3.3), simvastatin (aROR = 2.6; 1.6, 4.1), atorvastatin (aROR=3.4; 2.1, 5.4) and rosuvastatin (aROR = 7.1; 2.6, 19.4) [$p < 0.001$ for all] but not for pravastatin and fluvastatin. We did not find any relationship between the occurrence of ED and the daily dose or the duration of exposure to statins (data not shown).
- Assessment of the association between drugs other than statins known to be at risk of ED had confirmed a significant association for finasteride (aROR= 14.5; 95% CI 8.3, 25.4), fibrates (aROR=3.6; 2.6, 5.1), b-adrenergic receptor antagonists (aROR=1.5; 1.01, 2.1) and tricyclic antidepressants (aROR = 2.0; 1.2, 3.4) [all $p<0.05$].

Do et al. [190] made the ensuing conclusions:

- Despite some methodological limitations, their reported study had indicated that statins might induce or worsen ED in accordance with other data.
- Further pharmacology and epidemiological studies are necessary to confirm this conclusion and to improve the precision of the prevalence and/or the risk factors of this ADR.

Yassin et al. [191] made the ensuing iterations:

- Androgens are critical for the maintenance of penile structure and function and androgen deficiency alters the function of the corporal veno-occlusive mechanism in animal models.
- Nevertheless, there are limited research and data supporting this association in humans.

Yassin et al. [191] presented the case reports of hypogonadal men (N = 12) with low plasma testosterone and moderate to severe erectile dysfunction. Yassin et al. [] iterated that comorbidities had varied, including diabetes mellitus type I or II, metabolic syndrome with possible related hypertension, dyslipidaemia, or obesity. Oral phosphodiesterase type 5 (PDE5) inhibitor therapy had not improved the erectile function. Each patient had undergone baseline dynamic infusion pharmacocavernosometry and cavernosography which had demonstrated various degrees of corporal veno-occlusive dysfunction. The patients had undergone treatment with 1,000 mg injectable testosterone undecanoate (Nebido^{R}) on day 1, followed by another injection after 6 weeks and every 3 months thereafter. Dynamic infusion pharmacocavernosography was repeated in all 12 patients after 3 months of treatment. Yassin et al. [191] summated the results as follows:

- Five out of the 12 patients had reported significant improvement in their erectile function within 12 weeks to 20 weeks of androgen treatment and were at the time of publication of the article under follow-up assessments.
- Compared with baseline pharmacocavernosography, repeat radiology-image studies in patients who reported improvement in erectile function did not demonstrate veins draining the corporal bodies.
- The patients who responded to androgens also noted improvement in their sexual desire domain (International Index of Erectile Function [IIEF] scores which had increased from 4 ± 0.7 to 8 ± 0.3) and erectile function domain (IIEF scores which had increased from 6 ± 2 to 24 ± 1).

Yassin et al. [191] made the ensuing conclusions:

- The observations made in these limited series of case reports had indicated that testosterone improved erectile function in hypogonadal patients by restoring veno-occlusive function.
- Prospective, multi-institutional, double-blind placebo-controlled trials in hypogonadal patients are needed.

Dastoli et al. [192] made the ensuing iterations:

- Psoriasis is a cutaneous inflammatory condition, which is typified by an altered turnover of keratinocytes leading to scaly patches.
- Secukinumab and ixekizumab are two biologic medications that inhibit interleukin-17.

Dastoli et al. [192] reported the first case, according to Naranjo score, of a secukinumab-induced erectile dysfunction with severe plaque psoriasis which disappeared ensuing switching to another anti IL17 drug (ixekizumab). Dastoli et al. [192] reported a 45 years old man, who had experienced erectile dysfunction during treatment with an anti-IL17. The adverse effect appeared after 60 days of treatment with secukinumab and rapidly disappeared after he had discontinued the drug. All necessary urological exams were undertaken. Re-administration of secukinumab, due to the exacerbation of psoriasis, caused the same sexual dysfunction after 60 days. His switching his medication to ixekizumab had led to a resolution of the erectile dysfunction and a complete skin clearance. Dastoli et al. [192] concluded that:

- They had described for the first time a sexual dysfunction possibly due to secukinumab and its resolution after the switch to another similar but different drug, which had highlighted the potential difference between anti-IL17A drugs.

Omer et al. [193] made the ensuing iterations:

- Even though available treatments for erectile dysfunction (ED) had expanded, there had been a concomitant shift in the treatment paradigm.
- Newer treatment options focus upon disease modification and improving overall erectile function.

Omer et al. [193] reviewed the evidence of 3 promising novel ED treatments. Omer et al. [193] summated the results as follows:

- Li-ESWT section included 1 randomized controlled study, 2 prospective studies, 1 animal study, and 2 meta-analyses.
- IIEF score improvement was 3.54 (range 1.99–6.40). The authors concluded statistically significant short-term effect and improvement in erectile function (EF) with Li-ESWT.
- SCT section included 4 case series and 1 open-label study. Intraperitoneal, venous, and cavernosal SCT injections improved EF in animal models. 3 studies (n = 6–8) demonstrated 83–100% and 29–50% of patients regained erection and penetration ability, respectively. 2 studies (n = 12–16) found that all patients improved IIEF scores after SCT.
- Their literature review for PRP had yielded 3 animal, 1 retrospective, and 1 prospective study.
- Animal studies had demonstrated that rats sustaining crush cavernosal injuries which were treated with PRP significantly improved EF and preservation of cavernous nerve axons.
- One retrospective analysis on humans revealed mean improvement by 4.14 in IIEF scores.
- One prospective study on humans (n = 75) had demonstrated improved peak systolic velocity (P = .005) and IIEF scores (P = .046) with PRP therapy.

Omer et al. [193] made the ensuing conclusions:

- Their review, had demonstrated limited published evidence on current novel ED treatment options.
- Further research on Li-ESWT, SCT, and PRP therapy is required to ascertain the role of these therapies in ED treatment regimens.

Perry [194] made the ensuing iterations:

- Proton pump inhibitors are often used (and often overused) medications that have adverse effects including vitamin B12 deficiency, Clostridium difficile colitis, and increased risk of chronic kidney disease.
- Erectile dysfunction is largely unrecognized as an adverse effect of proton pump inhibitors despite increasing evidence that proton pump inhibitors might contribute to impaired nitric oxide generation and endothelial dysfunction.

Perry [194] reported a 38-year-old Caucasian man, who had mild hypertension and no other significant medical history, and who developed profound erectile dysfunction within 2 days of commencing over-the-counter omeprazole therapy, with his erectile function rapidly normalized following his discontinuation of the drug. At the time of the episode, the patient was on a stable dose of lisinopril and he was not taking any other

medications or supplements. During the 2 years following the episode, the patient had not had any further episode of erectile difficulties. Perry [194] made the ensuing conclusions:

- Further study of erectile dysfunction as an adverse effect of proton pump inhibitors is required.
- In the meantime, proton pump inhibitors should be considered to be a potential cause of erectile dysfunction in healthy young patients and as a cause or contributor to erectile dysfunction in older patients in whom erectile dysfunction is often attributed to age or comorbidities.

Deforge et al. [195] reviewed sexuality in persons with spinal cord injuries (SCIs), and reported the effectiveness of erectile interventions. Deforge et al. [195] screened reports from six databases (1966–2003), selected annual proceedings (1997–2002) and manufacturer's information against eligibility criteria. In the study, included reports were abstracted and data pooled from case-series reports regarding intracavernous injections and sildenafil. Deforge et al. [195] summarised the results as follows:

- From 2127 unique reports that they had evaluated, 49 were included.
- Male sexual dysfunction was addressed in these reports of several interventions including behavioural therapy, topical agents, intraurethral alprosatadil, intracavernous injections, vacuum tumescence devices, penile implants, sacral stimulators and oral medication.
- Penile injections resulted in successful erectile function in 90% (95% CI: 83%, 97%) of the men.
- Sildenafil resulted in 79% (95% CI: 68%, 90%) success; the difference in efficacy was not statistically significant.
- Five case-series reports which involved 363 participants with penile implants had shown a high satisfaction rate, but a 10% complication rate.

Deforge et al. [195] made the ensuing conclusions:

- A large body of evidence addressing sexuality in males had focussed upon erection.
- Penile injection, sildenafil and vacuum devices generally had obviated the need for penile implant insertions to address erectile dysfunction.
- Interventions might positively affect sexual activity in the short term.
- Long-term sexual adjustment and holistic approaches beyond erections had remained to be studied.
- Rigorous study design and reporting, using common outcome measures, would facilitate higher quality research. This would positively impact the care of patients.

Fraunfelder [196] described the known ocular side effects of agents that are used to treat erectile dysfunction. Fraunfelder [196] undertook a review of 892 case reports from the National Registry of Drug-Induced Ocular Side Effects (Casey Eye Institute, Portland, Oregon), the Food and Drug Administration (FDA), and the World Health Organization (WHO) and conducted a comprehensive review of the literature. Fraunfelder [196] summarised the results as follows:

- Ocular side effects of these drugs appear fully reversible and transitory.

Fraunfelder [196] made the ensuing conclusions:

- Up to 2005, evidence had not existed to discourage the use of erectile dysfunction agents that are attributable to harmful ocular side effects.
- Ischemic optic neuropathy (ION) is “possible” by WHO classification; nevertheless, conclusive evidence linking ION to erectile dysfunction medications was still lacking.

Ludwig and Phillips. [1] made the ensuing iterations:

- There are a significant number of men under 40 who experience erectile dysfunction (ED).
- In the past, the vast majority of ED cases were thought to be psychogenic in nature.
- Studies had identified organic aetiologies in between 15% to 72% of men with ED under 40.
- Organic aetiologies of ED include: vascular, neurogenic, Francois Gigot dela Peyronie's disease (PD), medication side effects and endocrinologic sources.
- Vascular causes are commonly due to focal arterial occlusive disease.
- Young men with multiple sclerosis, epilepsy and trauma in close proximity to the spinal cord are at increased risk for the development of ED.
- It is estimated that 8% of men with PD are under 40, with 21% of these individuals experiencing ED.
- Medications that cause ED include: antidepressants, NSAIDs and finasteride (Propecia), antiepileptics and neuroleptics.
- Hormonal sources of ED are not common in the young population; nevertheless, possible aetiologies of ED include: Klinefelter's syndrome, congenital hypogonadotropic hypogonadism, and acquired hypogonadotropic hypogonadism.
- The workup assessments of young men with ED should include a thorough history and physical examination.
- The significant prevalence of vascular aetiologies of ED in young men should prompt consideration of nocturnal penile tumescence testing and penile Doppler ultrasound.
- Treatment options that might improve ED include exercise and oral PDE-5 inhibitors.

Summation

- Erectile dysfunction (ED) is a common male sexual dysfunction which is associated with a reduced quality of life for patients and their partners.
- ED is known to be associated with increasing age, depression, obesity, lack of exercise, diabetes mellitus, hypertension, dyslipidaemia, cardiovascular disease and lower urinary tract symptoms related to benign prostatic hyperplasia.
- The assessment of men who have ED entails a full medical and personally as well as culturally sensitive sexual history taking, a focused clinical examination, fasting blood glucose levels, a fasting lipid profile and, in select cases, a total serum testosterone level and a serum prostate-specific antigen testing
- Treatment of ED requires lifestyle modification, reduction of comorbid vascular risk factors, and treatment of organic or psychosexual dysfunction with either pharmacotherapy alone or in combination with psychosexual treatment.
- Between 60% and 65% of men who are afflicted by ED, including those who have hypertension, diabetes mellitus, spinal cord injury and other comorbid medical conditions, could successfully complete coital activity in response to the

phosphodiesterase type 5 inhibitors (PDE5i) sildenafil, tadalafil, vardenafil and avanafil.

- Patient-administered intracorporal injection treatment utilising vasodilator medicaments such as alprostadil is an effective treatment and is useful in men who fail to respond to oral pharmacological agents.
- Surgical therapy of ED with multicomponent inflatable penile implants is associated with variably / high satisfaction rates.
- Penile arterial revascularisation and venous ligation surgery are associated with relatively poor outcome results in men with penile atherosclerotic disease or corporal veno-occlusive dysfunction.

Conclusions

- ED is a common manifestation in the entire world and is associated with a reduced quality of life for the ED patient and their coital partners.
- ED is linked to several risk factors, including obesity, lack of exercise, diabetes mellitus, hypertension, dyslipidaemia, cardiovascular disease and cigarette smoking.
- ED could be the manifesting sign of generalised endothelial dysfunction and is a predictor of overall cardiovascular health and silent myocardial ischaemia.
- Treatment with ED pharmacotherapy alone or in combination with graded psychosexual therapy is effective in improving and/or restoring sexual function in most men.
- Overall, there is a high level of consensus opinion upon the management of ED in the selected guidelines with few inconsistencies.

Conflict Of Interest – Nil

Acknowledgements

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References

1. Ludwig W, Phillips M. Organic causes of erectile dysfunction in men under 40. Urologia internationalis. 2014 Jan 1;92(1):1-6.
2. Shamloul R, Ghanem H. Erectile dysfunction. 2013 Jan 12;381(9861):153-65.
3. dical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol. 1994 Jan;151(1):54-61.
4. Leslie S W, Sooriyamorthy T. Erectile Dysfunction. Stat Pearls National Library of Medicine National Center for Biotechnology Information. NIH. Last updated 2024 January 09.
5. Muneer A, Kalsi J, Nazareth I, Arya M. Erectile dysfunction. BMJ. 2014 Jan 27;348: g129.
6. Orimoloye OA, Feldman DI, Blaha MJ. (2019). Erectile dysfunction links to cardiovascular disease-defining the clinical value. Trends Cardiovasc Med. Nov;29(8):458-465.
7. Miner M, Nehra A, Jackson G, Bhasin S, Billups K, Burnett AL, Buvat J, Carson C, Cunningham G, Ganz P, Goldstein I, Guay A, Hackett G, Kloner RA, Kostis JB, LaFlamme KE, Montorsi P, Ramsey M, Rosen R, Sadovsky R, Seftel A, Shabsigh R, Vlachopoulos C, Wu F. (2014). All men with vasculogenic erectile dysfunction require a cardiovascular workup. *Am J Med.* Mar;127(3):174-82.
8. Miner M, Parish SJ, Billups KL, Paulos M, Sigman M, Blaha MJ. Erectile Dysfunction and Subclinical Cardiovascular Disease. *Sex Med Rev.* 2019 Jul;7(3):455-463.
9. Corona G, Rastrelli G, Isidori AM, Pivonello R, Bettocchi C, et all., (2020). Erectile dysfunction and cardiovascular risk: a review of current findings. *Expert Rev Cardiovasc Ther*. Mar;18(3):155-164.
10. Randrup E, Baum N, Feibus A. (2015). Erectile dysfunction and cardiovascular disease. *Postgrad Med.* Mar;127(2):166-72
11. Matsui H, Sopko NA, Hannan JL, Bivalacqua TJ. (2015). Pathophysiology of erectile dysfunction. Curr Drug Targets.;16(5):411-419.
12. Kouidrat Y, Pizzol D, Cosco T, Thompson T, Carnaghi M, ET ALL., (2017). High prevalence of erectile dysfunction in diabetes: a systematic review and meta-analysis of 145 studies. Diabet Med. Sep;34(9):1185-1192
13. Razdan S, Greer AB, Patel A, Alameddine M, Jue JS, Ramasamy R. (2018). Effect of prescription medications on erectile dysfunction. *Postgrad Med J.* Mar;94(1109):171-178.
14. Mazzilli R, Angeletti G, Olana S, Delfino M, Zamponi V, et all., (2018). Erectile dysfunction in patients taking psychotropic drugs and treated with phosphodiesterase-5 inhibitors. *Arch Ital Urol Androl.* Mar 31;90(1):44-48.
15. Larson TR. Current treatment options for benign prostatic hyperplasia and their impact on sexual function. Urology. 2003 Apr;61(4):692-8.
16. Chen CM, Tsai MJ, Wei PJ, Su YC, Yang CJ, et all., (2015). Erectile Dysfunction in Patients with Sleep Apnea--A Nationwide Population-Based Study. *PLoS One*. Jul 15;10(7): e0132510.
17. Shen TC, Chen WC, Lin CL, Chen CH, Tu CY, ET ALL., (2015). The risk of erectile dysfunction in chronic obstructive pulmonary disease: a population-based cohort study in Taiwan. *Medicine* (Baltimore). Apr;94(14):e448.
18. Nathoo NA, Etminan M, Mikelberg FS. (2015). Association between glaucoma, glaucoma therapies, and erectile dysfunction. *J Glaucoma.* Feb;24(2):135-137.
19. Kupelian V, Link CL, McKinlay JB. (2007). Association between smoking, passive smoking, and erectile dysfunction: results from the Boston Area Community Health (BACH) Survey. *Eur Urol.* Aug;52(2):416-22.
20. Imamura M, Waseda Y, Marinova GV, Ishibashi T, Obayashi S, et all., (2007). arginase, and DDAH protein expression in rabbit cavernous tissue after administration of cigarette smoke extract. *Am J Physiol Regul Integr Comp Physiol*. Nov;293(5): R2081-2089.
21. Montorsi F, Briganti A, Salonia A, Rigatti P, Margonato A, et all., (2003). Erectile dysfunction prevalence, time of onset and association with risk factors in 300 consecutive patients with acute chest pain and angiographically documented coronary artery disease. *Eur Urol.* Sep;44(3):360-364; discussion 364-365.

22. Guay AT. (2005). Relation of endothelial cell function to erectile dysfunction: implications for treatment. *Am J Cardiol.* Dec 26;96(12B):52M-56M.
23. Imprialos K, Koutsampasopoulos K, Manolis A, Doumas M. (2021). Erectile Dysfunction as a Cardiovascular Risk Factor: Time to Step Up? *Curr Vasc Pharmacol*;19(3):301-312.
24. Inman BA, Sauver JL, Jacobson DJ, McGree ME, Nehra A, et all. (2009). A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. Mayo Clin Proc. Feb;84(2):108-113
25. Thompson IM, Tangen CM, Goodman PJ, Probstfield JL, Moinpour CM, Coltman CA. (2005). Erectile dysfunction and subsequent cardiovascular disease. *JAMA.* Dec 21;294(23):2996-3002.
26. Vlachopoulos CV, Terentes-Printzios DG, Ioakeimidis NK, Aznaouridis KA, Stefanadis CI. (2013). Prediction of cardiovascular events and all-cause mortality with erectile dysfunction: a systematic review and meta-analysis of cohort studies. *Circ Cardiovasc Qual Outcomes*. Jan 1;6(1):99-109.
27. Nehra A, Jackson G, Miner M, Billups KL, Burnett AL, Buvat J, Carson CC, Cunningham GR, Ganz P, Goldstein I, Guay AT, Hackett G, Kloner RA, Kostis J, Montorsi P, ET ALL., (2012). The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease. *Mayo Clin Proc*. Aug;87(8):766-778.
28. Nehra A, Jackson G, Miner M, Billups KL, Burnett AL, Buvat J, Carson CC, Cunningham GR, Goldstein I, Guay AT, Hackett G, Kloner RA, Kostis J, Montorsi P, Ramsey M, Rosen RC, Sadovsky R, Seftel AD, Vlachopoulos C, Wu FC. Diagnosis and treatment of erectile dysfunction for reduction of cardiovascular risk. J Urol. 2013 Jun;189(6):2031-8.
29. Jackson G, Nehra A, Miner M, Billups KL, Burnett AL, Buvat J, Carson CC, Cunningham G, Goldstein I, Guay AT, Hackett G, Kloner RA, Kostis JB, Montorsi P, Ramsey M, Rosen R, Sadovsky R, Seftel AD, Shabsigh R, Vlachopoulos C, Wu FC. The assessment of vascular risk in men with erectile dysfunction: the role of the cardiologist and general physician. Int J 0PMID: 23714173.
30. Seftel AD, Sun P, Swindle R. The prevalence of hypertension, hyperlipidemia, diabetes mellitus and depression in men with erectile dysfunction. J Urol. 2004 Jun;171(6 Pt 1):2341-5.
31. Rosen RC, Fisher WA, Eardley I, Niederberger C, Nadel A, Sand M; Men's Attitudes to Life Events and Sexuality (MALES) Study. The multinational Men's Attitudes to Life Events and Sexuality (MALES) study: I. Prevalence of erectile dysfunction and related health concerns in the general population. Curr Med Res Opin. 2004 May;20(5):607-17.
32. Manolis A, Doumas M. Sexual dysfunction: the 'prima ballerina' of hypertension-related quality-of-life complications. J Hypertens. 2008 Nov;26(11):2074-84. doi: 10.1097/HJH.0b013e32830dd0c6. PMID: 18854743.
33. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol. 1994 Jan;151(1):54-61.
34. Skeldon SC, Detsky AS, Goldenberg SL, Law MR. Erectile Dysfunction and Undiagnosed Diabetes, Hypertension, and Hypercholesterolemia. Ann Fam Med. 2015 Jul-Aug;13(4):331-5.
35. Eaton CB, Liu YL, Mittleman MA, Miner M, Glasser DB, Rimm EB. A retrospective study of the relationship between biomarkers of atherosclerosis and erectile dysfunction in 988 men. Int J Impot Res. 2007 Mar-Apr;19(2):218-25.
36. Dhindsa S, Prabhakar S, Sethi M, Bandyopadhyay A, Chaudhuri A, Dandona P. Frequent occurrence of hypogonadotropic hypogonadism in type 2 diabetes. J Clin Endocrinol Metab. 2004 Nov;89(11):5462-8.
37. Slag MF, Morley JE, Elson MK, Trence DL, Nelson CJ, Nelson AE, Kinlaw WB, Beyer HS, Nuttall FQ, Shafer RB. Impotence in medical clinic outpatients. JAMA. 1983 Apr 1;249(13):1736-40. PMID: 6827762.
38. Araujo AB, Esche GR, Kupelian V, O'Donnell AB, Travison TG, Williams RE, Clark RV, McKinlay JB. Prevalence of symptomatic androgen deficiency in men. J Clin Endocrinol Metab. 2007 Nov;92(11):4241-7.
39. Wu FC, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, O'Neill TW, Bartfai G, Casanueva FF, Forti G, Giwercman A, Han TS, Kula K, Lean ME, Pendleton N, Punab M, Boonen S, Vanderschueren D, Labrie F, Huhtaniemi IT; EMAS Group. Identification of late-onset hypogonadism in middle-aged and elderly men. N Engl J Med. 2010 Jul 8;363(2):123-35.
40. Janiszewski PM, Janssen I, Ross R. Abdominal obesity and physical inactivity are associated with erectile dysfunction independent of body mass index. J Sex Med. 2009 Jul;6(7):1990-8
41. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol. 1999 Apr;19(4):972-8.
42. Pourmand G, Alidaee MR, Rasuli S, Maleki A, Mehrsai A. Do cigarette smokers with erectile dysfunction benefit from stopping? a prospective study. BJU Int. 2004 Dec;94(9):1310-3.
43. Meirelles RJA, Lizarte Neto FS, Cirino MLA, Novais PC, Gula IS, Silva JPD, Tazzima MFGS, Fazan VPS, Durand MT, Tirapelli DPDC, Carvalho CAM, Schimming BC, Molina CAF, Tucci Junior S, Tirapelli LF. Morphological and molecular analysis of apoptosis in the corpus cavernosum of rats submitted to a chronic alcoholism model. Acta Cir Bras. 2020 Jun 3;35(3):e202000305.
44. Braun MH, Sommer F, Haupt G, Mathers MJ, Reifenrath B, Engelmann UH. Lower urinary tract symptoms and erectile dysfunction: co-morbidity or typical "Aging Male" symptoms? Results of the "Cologne Male Survey". Eur Urol. 2003 Nov;44(5):588-94.
45. Hoesl CE, Woll EM, Burkart M, Altwein JE. Erectile dysfunction (ED) is prevalent, bothersome and underdiagnosed in patients consulting urologists for benign prostatic syndrome (BPS). Eur Urol. 2005 Apr;47(4):511-7.
46. Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, O'Leary MP, Puppo P, Robertson C, Giuliano F. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). Eur Urol. 2003 Dec;44(6):637-49.
47. Liu Q, Zhang Y, Wang J, Li S, Cheng Y, Guo J, Tang Y, Zeng H, Zhu Z. Erectile Dysfunction and Depression: A

Systematic Review and Meta-Analysis. J Sex Med. 2018 Aug;15(8):1073-1082.
48. Fahmy A, Abdeldaiem H, Abdelsattar M, Aboyoussif T, Assem A, Zahran A, Elgebaly O. Impact of Bariatric Surgery on Sexual Dysfunction in Obese Men. Sex Med. 2021 Apr;9(2):100322.
49. Arolfo S, Scozzari G, Di Benedetto G, Vergine V, Morino M. Surgically induced weight loss effects on sexual quality of life of obese men: a prospective evaluation. Surg Endosc. 2020 Dec;34(12):5558-5565.
50. Groutz A, Gordon D, Schachter P, Amir H, Shimonov M. Effects of bariatric surgery on male lower urinary tract symptoms and sexual function. Neurourol Urodyn. 2017 Mar;36(3):636-639.
51. Corona G, Rastrelli G, Limoncin E, Sforza A, Jannini EA, Maggi M. Interplay Between Premature Ejaculation and Erectile Dysfunction: A Systematic Review and Meta-Analysis. J Sex Med. 2015 Dec;12(12):2291-300.
52. Wein AJ, Van Arsdalen KN. Drug-induced male sexual dysfunction. Urol Clin North Am. 1988 Feb;15(1):23-31. PMID: 3278473.
53. Ko DT, Hebert PR, Coffey CS, Sedrakyan A, Curtis JP, Krumholz HM. Beta-blocker therapy and symptoms of depression, fatigue, and sexual dysfunction. JAMA. 2002 Jul 17;288(3):351-7.
54. Kirby RS, O'Leary MP, Carson C. Efficacy of extended-release doxazosin and doxazosin standard in patients with concomitant benign prostatic hyperplasia and sexual dysfunction. BJU Int. 2005 Jan;95(1):103-9; discussion 109.
55. Hunt AA, Choudhury KR, Nukala V, Nolan MW, Ahmad A, Ashcraft KA, Koontz BF. Risk of erectile dysfunction after modern radiotherapy for intact prostate cancer. Prostate Cancer Prostatic Dis. 2021 Mar;24(1):128-134.
56. Emanu JC, Avildsen IK, Nelson CJ. Erectile dysfunction after radical prostatectomy: prevalence, medical treatments, and psychosocial interventions. Curr Opin Support Palliat Care. 2016 Mar;10(1):102-7.
57. Schwarzer U, Sommer F, Klotz T, Cremer C, Engelmann U. Cycling and penile oxygen pressure: the type of saddle matters. Eur Urol. 2002 Feb;41(2):139-43.
58. Balasubramanian A, Yu J, Breyer BN, Minkow R, Eisenberg ML. The Association Between Pelvic Discomfort and Erectile Dysfunction in Adult Male Bicyclists. J Sex Med. 2020 May;17(5):919-929.
59. Gan ZS, Ehlers ME, Lin FC, Wright ST, Figler BD, Coward RM. Systematic Review and Meta-Analysis of Cycling and Erectile Dysfunction. Sex Med Rev. 2021 Apr;9(2):304-311.
60. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, Maggi M, Nelson CJ, Parish S, Salonia A, Tan R, Mulhall JP, Hellstrom WJ. Erectile dysfunction. Nat Rev Dis Primers. 2016 Feb 4; 2:16003.
61. McKinlay JB. The worldwide prevalence and epidemiology of erectile dysfunction. Int J Impot Res. 2000 Oct;12 Suppl 4: S6-S11.
62. Ayta IA, McKinlay JB, Krane RJ. The likely worldwide increase in erectile dysfunction between 1995 and 2025 and some possible policy consequences. BJU Int. 1999 Jul;84(1):50-6.
63. Laumann EO, Paik A, Rosen RC. The epidemiology of erectile dysfunction: results from the National Health and Social Life Survey. Int J Impot Res. 1999 Sep;11 Suppl 1: S60-4.
64. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. JAMA. 1999 Feb 10;281(6):537-44.
65. Dean RC, Lue TF. Physiology of penile erection and pathophysiology of erectile dysfunction. Urol Clin North Am. 2005 Nov;32(4):379-95, v..
66. Ignarro LJ, Bush PA, Buga GM, Wood KS, Fukuto JM, Rajfer J. Nitric oxide and cyclic GMP formation upon electrical field stimulation cause relaxation of corpus cavernosum smooth muscle. Biochem Biophys Res Commun. 1990 Jul 31;170(2):843-50.
67. Giuliano F. Neurophysiology of erection and ejaculation. J Sex Med. 2011 Oct;8 Suppl 4:310-5.
68. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, Heidelbaugh J, Khera M, McVary KT, Miner MM, Nelson CJ, Sadeghi-Nejad H, Seftel AD, Shindel AW. Erectile Dysfunction: AUA Guideline. J Urol. 2018 Sep;200(3):633-641.
69. Neijenhuijs KI, Holtmaat K, Aaronson NK, Holzner B, Terwee CB, Cuijpers P, Verdonck-de Leeuw IM. The International Index of Erectile Function (IIEF)-A Systematic Review of Measurement Properties. J Sex Med. 2019 Jul;16(7):1078-1091.
70. Chrysant SG. Antihypertensive therapy causes erectile dysfunction. Curr Opin Cardiol. 2015 Jul;30(4):383-90.
71. Leiblum SR, Rosen RC. Couples therapy for erectile disorders: conceptual and clinical considerations. J Sex Marital Ther. 1991 Summer;17(2):147-59.
72. Marwick C. Survey says patients expect little physician help on sex. JAMA. 1999 Jun 16;281(23):2173-4.
73. Bodie JA, Beeman WW, Monga M. Psychogenic erectile dysfunction. Int J Psychiatry Med. 2003;33(3):273-93.
74. Hawton K, Catalan J, Fagg J. Sex therapy for erectile dysfunction: characteristics of couples, treatment outcome, and prognostic factors. Arch Sex Behav. 1992 Apr;21(2):161-75.
75. Melnik T, Soares BG, Nasello AG. The effectiveness of psychological interventions for the treatment of erectile dysfunction: systematic review and meta-analysis, including comparisons to sildenafil treatment, intracavernosal injection, and vacuum devices. J Sex Med. 2008 Nov;5(11):2562-74.
76. Domes T, Najafabadi BT, Roberts M, Campbell J, Flannigan R, Bach P, Patel P, Langille G, Krakowsky Y, Violette PD. Canadian Urological Association guideline: Erectile dysfunction. Can Urol Assoc J. 2021 Oct;15(10):310-322..
77. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, Cording E, Tomson D, Dodd C, Rollnick S, Edwards A, Barry M. Shared decision making: a model for clinical practice. J Gen Intern Med. 2012 Oct;27(10):1361-7.
78. Breda G, Xausa D, Giunta A, Tamai A, Silvestre P, Gherardi L. Nomogram for penile biothesiometry. Eur Urol. 1991;20(1):67-9.
79. Wiggins A, Farrell MR, Tsambarlis P, Levine LA. The Penile Sensitivity Ratio: A Novel Application of Biothesiometry to Assess Changes in Penile Sensitivity. J Sex Med. 2019 Mar;16(3):447-451.
80. Bemelmans BL, Hendrikx LB, Koldewijn EL, Lemmens WA, Debruyne FM, Meuleman EJ. Comparison of

biothesiometry and neuro-urophysiological investigations for the clinical evaluation of patients with erectile dysfunction. J Urol. 1995 May;153(5):1483-6. PMID: 7714973.
81. Suzuki K, Sato Y, Horita H, Adachi H, Kato R, Hisasue S, Itoh N, Tsukamoto T. The correlation between penile tumescence measured by the erectometer and penile rigidity by the RigiScan. Int J Urol. 2001 Nov;8(11):594-8.
82. Kwan M, Greenleaf WJ, Mann J, Crapo L, Davidson JM. The nature of androgen action on male sexuality: a combined laboratory-self-report study on hypogonadal men. J Clin Endocrinol Metab. 1983 Sep;57(3):557-62.
83. Fenwick PB, Mercer S, Grant R, Wheeler M, Nanjee N, Toone B, Brown D. Nocturnal penile tumescence and serum testosterone levels. Arch Sex Behav. 1986 Feb;15(1):13-21
84. Varela CG, Yeguas LAM, Rodríguez IC, Vila MDD. Penile Doppler Ultrasound for Erectile Dysfunction: Technique and Interpretation. AJR Am J Roentgenol. 2020 May;214(5):1112-1121.
85. Quam JP, King BF, James EM, Lewis RW, Brakke DM, Ilstrup DM, Parulkar BG, Hattery RR. Duplex and color Doppler sonographic evaluation of vasculogenic impotence. AJR Am J Roentgenol. 1989 Dec;153(6):1141-7.
86. Jung DC, Park SY, Lee JY. Penile Doppler ultrasonography revisited. Ultrasonography. 2018 Jan;37(1):16-24.
87. Naroda T, Yamanaka M, Matsushita K, Kimura K, Kawanishi Y, Numata A, Yuasa M, Tamura M, Kagawa S. [Clinical studies for venogenic impotence with color Doppler ultrasonography--evaluation of resistance index of the cavernous artery]. Nihon Hinyokika Gakkai Zasshi. 1996 Nov;87(11):1231-5. Japanese.
88. Ma M, Yu B, Qin F, Yuan J. Current approaches to the diagnosis of vascular erectile dysfunction. Transl Androl Urol. 2020 Apr;9(2):709-721
89. Ford PL. Dynamic infusion cavernosometry and cavernosography. Urol Nurs. 2000 Aug;20(4):239-40, 243, 253; quiz 244-5. PMID: 11998086.
90. Gao QQ, Chen JH, Chen Y, Song T, Dai YT. Dynamic infusion cavernosometry and cavernosography for classifying venous erectile dysfunction and its significance for individual treatment. Chin Med J (Engl). 2019 Feb;132(4):405-410.
91. Pereira JA, Bilhim T, Rio Tinto H, Fernandes L, Martins Pisco J, Goyri-O'Neill J. Radiologic anatomy of arteriogenic erectile dysfunction: a systematized approach. Acta Med Port. 2013 May-Jun;26(3):219-25. Epub 2013 Jun 28. PMID: 23815835.
92. La Vignera S, Condorelli RA, Cannarella R, Giacone F, Calogero AE. Arterial erectile dysfunction is an early sign of vascular damage: the importance for the prevention of cardiovascular health. Ann Transl Med. 2019 Jul;7(Suppl 3):S124.
93. Rhim HC, Kim MS, Park YJ, Choi WS, Park HK, Kim HG, Kim A, Paick SH. The Potential Role of Arginine Supplements on Erectile Dysfunction: A Systemic Review and Meta-Analysis. J Sex Med. 2019 Feb;16(2):223-234. doi: 10.1016/j.jsxm.2018.12.002. Erratum in: J Sex Med. 2020 Mar;17(3):560.
94. Khera M, Goldstein I. Erectile dysfunction. BMJ Clin Evid. 2011 Jun 29; 2011:1803. PMID: 21711956; PMCID: PMC3217797.
95. Goldstein I, Tseng LJ, Creanga D, Stecher V, Kaminetsky JC. Efficacy and Safety of Sildenafil by Age in Men With Erectile Dysfunction. J Sex Med. 2016 May;13(5):852-9.
96. Wolfe SM. There have been inadequate warnings that erectile dysfunction drugs can cause blindness. MedGenMed. 2005 Dec 5;7(4):61. PMID: 16614683; PMCID: PMC1681722.
97. Pomeranz HD. Erectile Dysfunction Agents and Nonarteritic Anterior Ischemic Optic Neuropathy. Neurol Clin. 2017 Feb;35(1):17-27.
98. Thakur JS, Thakur S, Sharma DR, Mohindroo NK, Thakur A, Negi PC. Hearing loss with phosphodiesterase-5 inhibitors: a prospective and objective analysis with tadalafil. Laryngoscope. 2013 Jun;123(6):1527-30.
99. Khan AS, Sheikh Z, Khan S, Dwivedi R, Benjamin E. Viagra deafness--sensorineural hearing loss and phosphodiesterase-5 inhibitors. Laryngoscope. 2011 May;121(5):1049-54. doi: 10.1002/lary.21450. PMID: 21520123.
100. Maddox PT, Saunders J, Chandrasekhar SS. Sudden hearing loss from PDE-5 inhibitors: A possible cellular stress etiology. Laryngoscope. 2009 Aug;119(8):1586-9.
101. Foresta C, Caretta N, Rossato M, Garolla A, Ferlin A. Role of androgens in erectile function. J Urol. 2004 Jun;171(6 Pt 1):2358-62, quiz 2435.
102. Gallo L, Pecoraro S, Sarnacchiaro P, Silvani M, Antonini G. The Daily Therapy With L-Arginine 2,500 mg and Tadalafil 5 mg in Combination and in Monotherapy for the Treatment of Erectile Dysfunction: A Prospective, Randomized Multicentre Study. Sex Med. 2020 Jun;8(2):178-185.
103. Xu Z, Liu C, Liu S, Zhou Z. Comparison of efficacy and safety of daily oral L-arginine and PDE5Is alone or combination in treating erectile dysfunction: A systematic review and meta-analysis of randomised controlled trials. Andrologia. 2021 May;53(4):e14007.
104. SM, Storer TW, Anton S, Basaria S, Diem SJ, Hou X, Mohler ER 3rd, Parsons JK, Wenger NK, Zeldow B, Landis JR, Ellenberg SS; Testosterone Trials Investigators. Effects of Testosterone Treatment in Older Men. N Engl J Med. 2016 Feb 18;374(7):611-24.
105. Brock G, Heiselman D, Maggi M, Kim SW, Rodríguez Vallejo JM, Behre HM, McGettigan J, Dowsett SA, Hayes RP, Knorr J, Ni X, Kinchen K. Effect of Testosterone Solution 2% on Testosterone Concentration, Sex Drive and Energy in Hypogonadal Men: Results of a Placebo Controlled Study. J Urol. 2016 Mar;195(3):699-705.
106. Corona G, Rastrelli G, Morgentaler A, Sforza A, Mannucci E, Maggi M. Meta-analysis of Results of Testosterone Therapy on Sexual Function Based on International Index of Erectile Function Scores. Eur Urol. 2017 Dec;72(6):1000-1011.
107. Mulligan T, Frick MF, Zuraw QC, Stemhagen A, McWhirter C. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. Int J Clin Pract. 2006 Jul;60(7):762-9. 16846397; PMCID: PMC1569444.
108. It has been iterated that testosterone monotherapy is not considered an effective treatment for ED. [68] [66] [68] Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, Heidelbaugh J, Khera M, McVary KT, Miner MM, Nelson CJ, Sadeghi-Nejad H, Seftel AD, Shindel AW. Erectile Dysfunction: AUA Guideline. J Urol. 2018 Sep;200(3):633-641. doi: 10.1016/j.juro.2018.05.004.

Epub 2018 May 7. Erratum in: J Urol. 2022 Mar;207(3):743.
109. Khayyamfar F, Forootan SK, Ghasemi H, Miri SR, Farhadi E. Evaluating the efficacy of vacuum constrictive device and causes of its failure in impotent patients. Urol. J. 2014 Jan 4;10(4):1072-8. PMID: 24469653.
110. Williams G, Abbou CC, Amar ET, Desvaux P, Flam TA, Lycklama à Nijeholt GA, Lynch SF, Morgan RJ, Müller SC, Porst H, Pryor JP, Ryan P, Witzsch UK, Hall MM, Place VA, Spivack AP, Gesundheit N. Efficacy and safety of transurethral alprostadil therapy in men with erectile dysfunction. MUSE Study Group. Br J Urol. 1998 Jun;81(6):889-94.
111. Padma-Nathan H, Hellstrom WJ, Kaiser FE, Labasky RF, Lue TF, Nolten WE, Norwood PC, Peterson CA, Shabsigh R, Tam PY, Place VA, Gesundheit N. Treatment of men with erectile dysfunction with transurethral alprostadil. Medicated Urethral System for Erection (MUSE) Study Group. N Engl J Med. 1997 Jan 2;336(1):1-7.
112. Goldstein I, Payton T, Padma-Nathan H. Therapeutic roles of intracavernosal papaverine. Cardiovasc Intervent Radiol. 1988 Aug;11(4):237-9.
113. Duncan C, Omran GJ, Teh J, Davis NF, Bolton DM, Lawrentschuk N. Erectile dysfunction: a global review of intracavernosal injectables. World J Urol. 2019 Jun;37(6):1007-1014.
114. Hedlund H, Hedlund P. Pharmacotherapy in erectile dysfunction agents for self-injection programs and alternative application models. Scand J Urol Nephrol Suppl. 1996; 179:129-38. PMID: 8908679.
115. Armstrong DK, Convery A, Dinsmore WW. Intracavernosal papaverine and phentolamine for the medical management of erectile dysfunction in a genitourinary clinic. Int J STD AIDS. 1993 Jul-Aug;4(4):214-6.
116. Govier FE, McClure RD, Weissman RM, Gibbons RP, Pritchett TR, Kramer-Levien D. Experience with triple-drug therapy in a pharmacological erection program. J Urol. 1993 Dec;150(6):1822-4.
117. Shenfeld O, Hanani J, Shalhav A, Vardi Y, Goldwasser B. Papaverine-phentolamine and prostaglandin E1 versus papaverine-phentolamine alone for intracorporeal injection therapy: a clinical double-blind study. J Urol. 1995 Sep;154(3):1017-9. PMID: 7637045.
118. Linet OI, Ogrinc FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. The Alprostadil Study Group. N Engl J Med. 1996 Apr 4;334(14):873-7.
119. Silberman M, Stormont G, Leslie SW, Hu EW. Priapism. 2023 May 30. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 29083574.
120. Reece C, Kumar R, Nienow D, Nehra A. Extending the rationale of combination therapy to unresponsive erectile dysfunction. Rev Urol. 2007 Fall;9(4):197-206. PMID: 18231616; PMCID: PMC2213890.
121. Gutierrez P, Hernandez P, Mas M. Combining programmed intracavernous PGE1 injections and sildenafil on demand to salvage sildenafil non responders. Int J Impot Res. 2005 Jul-Aug;17(4):354-8.
122. Moncada I, Martinez-Salamanca J, Ruiz-Castañe E, Romero J. Combination therapy for erectile dysfunction involving a PDE5 inhibitor and alprostadil. Int J Impot Res. 2018 Oct;30(5):203-208.
123. Mydlo JH, Viterbo R, Crispen P. Use of combined intracorporal injection and a phosphodiesterase-5 inhibitor therapy for men with a suboptimal response to sildenafil and/or vardenafil monotherapy after radical retropubic prostatectomy. BJU Int. 2005 Apr;95(6):843-6.
124. Al-Adl AM, Abdel-Wahab O, El-Karamany T, Aal AA. Combined intracavernous vasoactive drugs and sildenafil citrate in treatment of severe erectile dysfunction not responding to on-demand monotherapy. Arab J Urol. 2011 Jun;9(2):153-8. doi: 10.1016/j.aju.2011.06.008. Epub 2011 Sep 15. PMID: 26579288; PMCID: PMC4150578.
125. Yang Y, Hu JL, Ma Y, Wang HX, Chen Z, Xia JG, Wang YX, Huang YR, Chen B. Oral tadalafil administration plus low dose vasodilator injection: a novel approach to erection induction for penile color duplex ultrasound. J Urol. 2011 Jul;186(1):228-32.
126. Lee M, Sharifi R. Non-invasive Management Options for Erectile Dysfunction When a Phosphodiesterase Type 5 Inhibitor Fails. Drugs Aging. 2018 Mar;35(3):175-187. .
127. Khoudary KP, Morgentaler A. Design considerations in penile prostheses: the American Medical Systems product line. J Long Term Eff Med Implants. 1997;7(1):55-64. PMID: 10168541.
128. Levine LA, Estrada CR, Morgentaler A. Mechanical reliability and safety of, and patient satisfaction with the Ambicor inflatable penile prosthesis: results of a 2 center study. J Urol. 2001 Sep;166(3):932-7. PMID: 11490249.
129. Carson CC 3rd. Efficacy of antibiotic impregnation of inflatable penile prostheses in decreasing infection in original implants. J Urol. 2004 Apr;171(4):1611-4.
130. Hellstrom WJ, Hyun JS, Human L, Sanabria JA, Bivalacqua TJ, Leungwattanakij S. Antimicrobial activity of antibiotic-soaked, Resist-coated Bioflex. Int J Impot Res. 2003 Feb;15(1):18-21.
131. Wolter CE, Hellstrom WJ. The hydrophilic-coated inflatable penile prosthesis: 1-year experience. J Sex Med. 2004 Sep;1(2):221-4.
132. Wilson SK, Zumbe J, Henry GD, Salem EA, Delk JR, Cleves MA. Infection reduction using antibiotic-coated inflatable penile prosthesis. Urology. 2007 Aug;70(2):337-40.
133. Mulcahy JJ, Köhler TS, Wen L, Wilson SK. Penile implant infection prevention part II: device coatings have changed the game. Int J Impot Res. 2020 Dec;33(8):801-807.
134. Jarow JP. Risk factors for penile prosthetic infection. J Urol. 1996 Aug;156(2 Pt 1):402-4.
135. Wilson SK, Delk JR 2nd. Inflatable penile implant infection: predisposing factors and treatment suggestions. J Urol. 1995 Mar;153(3 Pt 1):659-61. PMID: 7861509.
136. Gurtner K, Saltzman A, Hebert K, Laborde E. Erectile Dysfunction: A Review of Historical Treatments With a Focus on the Development of the Inflatable Penile Prosthesis. Am J Mens Health. 2017 May;11(3):479-486.
137. Ji YS, Ko YH, Song PH, Moon KH. Long-term survival and patient satisfaction with inflatable penile prosthesis for the treatment of erectile dysfunction. Korean J Urol. 2015 Jun;56(6):461-5.
138. Chierigo F, Capogrosso P, Dehò F, Pozzi E, Schifano N, Belladelli F, Montorsi F, Salonia A. Long-Term Follow-Up After Penile Prosthesis Implantation-Survival and Quality of Life Outcomes. J Sex Med. 2019 Nov;16(11):1827-1833.

139. Molodysky E, Liu SP, Huang SJ, Hsu GL. Penile vascular surgery for treating erectile dysfunction: Current role and future direction. Arab J Urol. 2013 Sep;11(3):254-66. doi: 10.1016/j.aju.2013.05.001. Epub 2013 Jun 10. PMID: 26558090; PMCID: PMC4442997.
140. Diehm N, Do DD, Keo HH, Boerlin J, Regli C, Schumacher M, Jungmann PM, Raeber L, Baumann F. Early Recoil After Balloon Angioplasty of Erection-Related Arteries in Patients With Arteriogenic Erectile Dysfunction. J Endovasc Ther. 2018 Dec;25(6):710-715.
141. Wang TD, Lee WJ, Yang SC, Lin PC, Tai HC, Liu SP, Huang CH, Chen WJ, Chen MF, Hsieh JT. Clinical and Imaging Outcomes up to 1 Year Following Balloon Angioplasty for Isolated Penile Artery Stenoses in Patients With Erectile Dysfunction: The PERFECT-2 Study. J Endovasc Ther. 2016 Dec;23(6):867-877.
142. Diehm N, Marggi S, Ueki Y, Schumacher D, Keo HH, Regli C, Do DD, Moeltgen T, Grimsehl P, Wyler S, Schoenhofen H, Räber L, Schumacher M. Endovascular Therapy for Erectile Dysfunction-Who Benefits Most? Insights From a Single-Center Experience. J Endovasc Ther. 2019 Apr;26(2):181-190.
143. Hsu GL, Hsieh CH, Wen HS, Kang TJ, Chiang HS. Penile venous anatomy: application to surgery for erectile disturbance. Asian J Androl. 2002 Mar;4(1):61-6. PMID: 11907630.
144. Angulo JC, Arance I, de Las Heras MM, Meilán E, Esquinas C, Andrés EM. Efficacy of low-intensity shock wave therapy for erectile dysfunction: A systematic review and meta-analysis. Actas Urol Esp. 2017 Oct;41(8):479-490. English, Spanish.
145. Lu Z, Lin G, Reed-Maldonado A, Wang C, Lee YC, Lue TF. Low-intensity Extracorporeal Shock Wave Treatment Improves Erectile Function: A Systematic Review and Meta-analysis. Eur Urol. 2017 Feb;71(2):223-233.
146. Clavijo RI, Kohn TP, Kohn JR, Ramasamy R. Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis. J Sex Med. 2017 Jan;14(1):27-35.
147. Dong L, Chang D, Zhang X, Li J, Yang F, Tan K, Yang Y, Yong S, Yu X. Effect of A Systematic Review and Meta-Analysis. Am J Mens Health. 2019 Mar-Apr;13(2):1557988319846749.
148. Assaly-Kaddoum R, Giuliano F, Laurin M, Gorny D, Kergoat M, Bernabé J, Vardi Y, Alexandre L, Behr-Roussel D. Low Intensity Extracorporeal Shock Wave Therapy Improves Erectile Function in a Model of Type II Diabetes Independently of NO/cGMP Pathway. J Urol. 2016 Sep;196(3):950-6.
149. Liu MC, Chang ML, Wang YC, Chen WH, Wu CC, Yeh SD. Revisiting the Regenerative Therapeutic Advances Towards Erectile Dysfunction. Cells. 2020 May 19;9(5):1250. doi: 10.3390/cells9051250. PMID: 32438565; PMCID: PMC7290763.
150. Fojecki GL, Tiessen S, Osther PJ. Effect of Low-Energy Linear Shockwave Therapy on Erectile Dysfunction-A Double-Blinded, Sham-Controlled, Randomized Clinical Trial. J Sex Med. 2017 Jan;14(1):106-112.
151. Campbell JD, Trock BJ, Oppenheim AR, Anusionwu I, Gor RA, Burnett AL. Meta-analysis of randomized controlled trials that assess the efficacy of low-intensity shockwave therapy for the treatment of erectile dysfunction. Ther Adv Urol. 2019 Mar 29; 11:1756287219838364.
152. Vardi Y, Appel B, Kilchevsky A, Gruenwald I. Does low intensity extracorporeal shock wave therapy have a physiological effect on erectile function? Short-term results of a randomized, double-blind, sham controlled study. J Urol. 2012 May;187(5):1769-75.
153. Burnett AL, Rojanasarot S, Amorosi SL. An Analysis of a Commercial Database on the Use of Erectile Dysfunction Treatments for Men with Employer-Sponsored Health Insurance. Urology. 2021 Mar; 149:140-145.
154. Yiou R, Hamidou L, Birebent B, Bitari D, Lecorvoisier P, Contremoulins I, Khodari M, Rodriguez AM, Augustin D, Roudot-Thoraval F, de la Taille A, Rouard H. Safety of Intracavernous Bone Marrow-Mononuclear Cells for Postradical Prostatectomy Erectile Dysfunction: An Open Dose-Escalation Pilot Study. Eur Urol. 2016 Jun;69(6):988-91.
155. Yiou R, Hamidou L, Birebent B, Bitari D, Le Corvoisier P, Contremoulins I, Rodriguez AM, Augustin D, Roudot-Thoraval F, de la Taille A, Rouard H. Intracavernous Injections of Bone Marrow Mononucleated Cells for Postradical Prostatectomy Erectile Dysfunction: Final Results of the INSTIN Clinical Trial. Eur Urol Focus. 2017 Dec;3(6):643-645.
156. Masterson TA, Molina M, Ledesma B, Zucker I, Saltzman R, Ibrahim E, Han S, Reis IM, Ramasamy R. Platelet-rich Plasma for the Treatment of Erectile Dysfunction: A Prospective, Randomized, Double-blind, Placebo-controlled Clinical Trial. J Urol. 2023 Jul;210(1):154-161
157. Poulios E, Mykoniatis I, Pyrgidis N, Zilotis F, Kapoteli P, Kotsiris D, Kalyvianakis D, Hatzichristou D. Platelet-Rich Plasma (PRP) Improves Erectile Function: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial. J Sex Med. 2021 May;18(5):926-935..
158. Alkandari MH, Touma N, Carrier S. Platelet-Rich Plasma Injections for Erectile Dysfunction and Peyronie's Disease: A Systematic Review of Evidence. Sex Med Rev. 2022 Apr;10(2):341-352.
159. Israeli JM, Lokeshwar SD, Efimenko IV, Masterson TA, Ramasamy R. The potential of platelet-rich plasma injections and stem cell therapy for penile rejuvenation. Int J Impot Res. 2022 May;34(4):375-382.
160. Sari Motlagh R, Abufaraj M, Yang L, Mori K, Pradere B, Laukhtina E, Mostafaei H, Schuettfort VM, Quhal F, Montorsi F, Amjadi M, Gratzke C, Shariat SF. Penile Rehabilitation Strategy after Nerve Sparing Radical Prostatectomy: A Systematic Review and Network Meta-Analysis of Randomized Trials. J Urol. 2021 Apr;205(4):1018-1030.
161. Basal S, Wambi C, Acikel C, Gupta M, Badani K. Optimal strategy for penile rehabilitation after robot-assisted radical prostatectomy based on preoperative erectile function. BJU Int. 2013 Apr;111(4):658-65.
162. Liu C, Lopez DS, Chen M, Wang R. Penile Rehabilitation Therapy Following Radical Prostatectomy: A Meta-Analysis. J Sex Med. 2017 Dec;14(12):1496-1503.
163. Gabrielsen JS. Penile Rehabilitation: The "Up"-date. Curr Sex Health Rep. 2018 Dec;10(4):287-292.
164. Philippou YA, Jung JH, Steggall MJ, O'Driscoll ST, Bakker CJ, Bodie JA, Dahm P. Penile rehabilitation for postprostatectomy erectile dysfunction. Cochrane Database Syst Rev. 2018 Oct 23;10(10):CD012414.
165. Nicolai M, Urkmez A, Sarikaya S, Fode M, Falcone M, Albersen M, Gul M, Hatzichristodoulou G, Capogrosso P,

Russo GI. Penile Rehabilitation and Treatment Options for Erectile Dysfunction Following Radical Prostatectomy and Radiotherapy: A Systematic Review. Front Surg. 2021 Mar 2;8:636974.
166. Yuan J, Zhang R, Yang Z, Lee J, Liu Y, Tian J, Qin X, Ren Z, Ding H, Chen Q, Mao C, Tang J. Comparative effectiveness and safety of oral phosphodiesterase type 5 inhibitors for erectile dysfunction: a systematic review and network meta-analysis. Eur Urol. 2013 May;63(5):902-12.
167. Rezaee ME, Gross MS. Are We Overstating the Risk of Priapism With Oral Phosphodiesterase Type 5 Inhibitors? J Sex Med. 2020 Aug;17(8):1579-1582
168. Scherzer ND, Reddy AG, Le TV, Chernobylsky D, Hellstrom WJG. Unintended Consequences: A Review of Pharmacologically-Induced Priapism. Sex Med Rev. 2019 Apr;7(2):283-292.
169. Salonia A, Eardley I, Giuliano F, Hatzichristou D, Moncada I, Vardi Y, Wespes E, Hatzimouratidis K; European Association of Urology. European Association of Urology guidelines on priapism. Eur Urol. 2014 Feb;65(2):480-9.
170. [170] Corona G, Rastrelli G, Filippi S, Vignozzi L, Mannucci E, Maggi M. Erectile dysfunction and central obesity: an Italian perspective. Asian J Androl. 2014 Jul-Aug;16(4):581-91.
171. Ernst E, Pittler MH. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. J Urol. 1998 Feb;159(2):433-6.
172. Pittler MH, Ernst E. Trials have shown yohimbine is effective for erectile dysfunction. BMJ. 1998 Aug 15;317(7156):478.
173. Saad MA, Eid NI, Abd El-Latif HA, Sayed HM. Potential effects of yohimbine and sildenafil on erectile dysfunction in rats. Eur J Pharmacol. 2013 Jan 30;700(1-3):127-33.
174. Jaffer KY, Chang T, Vanle B, Dang J, Steiner AJ, Loera N, Abdelmesseh M, Danovitch I, Ishak WW. Trazodone for Insomnia: A Systematic Review. Innov Clin Neurosci. 2017 Aug 1;14(7-8):24-34. PMID: 29552421; PMCID: PMC5842888.
175. Hewett ML. What is causing this patient's priapism? JAAPA. 2015 Oct;28(10):59-60.
176. Saenz de Tejada I, Ware JC, Blanco R, Pittard JT, Nadig PW, Azadzoi KM, Krane RJ, Goldstein I. Pathophysiology of prolonged penile erection associated with trazodone use. J Urol. 1991 Jan;145(1):60-4.
177. Chiang PH, Tsai EM, Chiang CP. The role of trazodone in the treatment of erectile dysfunction. Gaoxiong Yi Xue Ke Xue Za Zhi. 1994 Jun;10(6):287-94. PMID: 8057411.
178. Fink HA, MacDonald R, Rutks IR, Wilt TJ. Trazodone for erectile dysfunction: a systematic review and meta-analysis. BJU Int. 2003 Sep;92(4):441-6.
179. Khera M, Albersen M, Mulhall JP. Mesenchymal stem cell therapy for the treatment of erectile dysfunction. J Sex Med. 2015 May;12(5):1105-6.
180. Lue TF. Erectile dysfunction. New England journal of medicine. 2000 Jun 15;342(24):1802-13.
181. Rew KT, Heidelbaugh JJ. Erectile dysfunction. American family physician. 2016 Nov 15;94(10):820-7. cureus.com/users/sign in
182. Wessells H, Joyce GF, Wise M, Wilt TJ. Erectile dysfunction. The Journal of urology. 2007 May 1;177(5):1675-1681.
183. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. The American journal of medicine. 2007 Feb 1;120(2):151-7.
184. Rossi M, Pellegrino M. Acitretin-associated erectile dysfunction: a case report. Cases journal. 2009 Dec; 2:1-3.
185. Beach RA, Murphy F, Vender RB. Cutaneous reaction to drugs used for erectile dysfunction: case report and review of the literature. Journal of Cutaneous Medicine and Surgery. 2006 May;10(3):128-30.
186. Badal J, Ramasamy R, Hakky T, Chandrashekar A, Lipshultz L. Case Report: Persistent erectile dysfunction in a man with prolactinoma. F1000Res. 2015 Jan 15; 4:13. doi: 10.12688/f1000research.5743.1. PMID: 25844161; PMCID: PMC4367515.
187. Heo SB, Park WY, Kim JH, Yoon KB. Back pain with erectile dysfunction: A case report. Anesthesia and Pain Medicine. 2012 Jul 31;7(3):217-20.
188. Heo SB, Park WY, Kim JH, Yoon KB. Back pain with erectile dysfunction: A case report. Anesthesia and Pain Medicine. 2012 Jul 31;7(3):217-20.
189. Hitiris N, Barrett JA, Brodie MJ. Erectile dysfunction associated with pregabalin add-on treatment in patients with partial seizures: five case reports. Epilepsy & Behavior. 2006 Mar 1;8(2):418-21.
190. Androshchuk V, Pugh N, Wood A, Ossei-Gerning N. Erectile dysfunction: a window to the heart. BMJ Case Rep. 2015 Apr 28;2015: bcr2015210124.
191. Do C, Huyghe E, Lapeyre-Mestre M, Montastruc JL, Bagheri H. Statins and erectile dysfunction: results of a case/non-case study using the French Pharmacovigilance System Database. Drug safety. 2009 Jul;32:591-7.
192. Yassin AA, Saad F, Traish A. Testosterone undecanoate restores erectile function in a subset of patients with venous leakage: a series of case reports. The journal of sexual medicine. 2006 Jul;3(4):727-35
193. Dastoli S, Iannone LF, Bennardo L, Silvestri M, Palleria C, Nisticò SP, De Sarro G, Russo E. A rare case of drug-induced erectile dysfunction with secukinumab solved after switch to ixekizumab in a psoriatic patient: a case report. Current Drug Safety. 2020 Mar 1;15(1):69-72.
194. Omer A. Raheem, Caleb Natale, Brian Dick, Amit G. Reddy, Ayad Yousif, Mohit Khera, Neil Baum, Novel Treatments of Erectile Dysfunction: Review of the Current Literature, *Sexual Medicine Reviews*, Volume 9, Issue 1, January 2021, Pages 123–132,
195. Perry TW. Abrupt-onset, profound erectile dysfunction in a healthy young man after initiating over-the-counter omeprazole: a case report. Journal of Medical Case Reports. 2021 Dec; 15:1-3.
196. Deforge D, Blackmer J, Garritty C, Yazdi F, Cronin V, Barrowman N, Fang M, Mamaladze V, Zhang L, Sampson M, Moher D. Male erectile dysfunction following spinal cord injury: a systematic review. Spinal cord. 2006 Aug;44(8):465-73.
197. Frederick W. Fraunfelder, Visual Side Effects Associated with Erectile Dysfunction Agents. American Journal of Ophthalmology. 2005; 140(4): 723-724, ISSN 0002-9394,