Current Sexual Health Reports (2019) 11:370–380
https://doi.org/10.1007/s11930-019-00220-z

FEMALE SEXUAL DYSFUNCTION AND DISORDERS (A PASTUSZAK AND N THIRUMAVALAVAN, SECTION EDITORS)

Management of the Acute Phase of Peyronie's Disease: a Contemporary Review

Dyvon T. Walker[1] · Arash Amighi[1] · Steven A. Mills[1] · Sriram V. Eleswarapu[1] · Jesse N. Mills[1]

Published online: 22 November 2019

Abstract

Purpose of Review The goal of this article is to review the current management options for Peyronie's disease (PD), focusing on the acute phase of the disease. Additionally, we aim to highlight the most recent literature on the subject.

Recent Findings Contemporary studies suggest that there are promising novel therapies on the horizon for acute phase PD, such as topical H-100 gel and intralesional interferon-α2b and mycophenolate mofetil. Recent findings also suggest that intralesional collagenase *Clostridium histolyticum* (CCH) may be effective for the acute phase of PD, in addition to its conventional use in the chronic phase.

Summary A variety of treatments have been proposed for PD, with more recent literature focusing on the acute phase. Novel topical therapies are on the horizon and may show promise. External mechanical therapies have shown clinically meaningful changes. CCH may have efficacy during the acute phase of PD. Other intralesional therapies are promising but still require additional large studies to confirm efficacy. Future research on the acute phase of PD may expand treatment options and impact disease management.

Keywords Peyronie's disease · Acute phase · Intralesional injection · Collagenase *Clostridium histolyticum*

Introduction

Peyronie's disease (PD) is a chronic inflammatory disease involving the tunica albuginea of the penis in which progressive fibrosis leads to plaque formation. The etiology is thought to be multifactorial and includes singular or repetitive trauma to the penis, genetic factors, inflammatory predispositions, and vascular or metabolic associations; however, the pathogenesis of the disease remains uncertain. Plaque formation as a result of fibrosis often causes pain in the acute phase of PD, followed by curvature (Fig. 1a) and other deformities of the erect penis such as narrowing, indentation, hourglassing, and loss of penile length and girth. Although pain usually subsides as the acute phase ends, deformities persist into the chronic, stable phase of the disease.

The prevalence of PD is reported to be up to 3.2% of men in the USA, and up to 20.3% of men with metabolic comorbidities [1, 2]. PD deformities can have a considerable impact on a man's sexual function and the psychological and sexual well-being of his partner and himself. Approximately 48% of men with PD suffer from clinical depression and the overall prevalence of emotional and relationship problems attributable to PD has been estimated at 81% and 54%, respectively [3, 4]. One attributes these problems to the association of PD with erectile dysfunction (ED); 40–50% of men with PD present with concomitant ED [5].

A variety of treatment options have been proposed for PD, but the disease remains a therapeutic challenge for urologists; there is no definitive surgical or non-surgical cure, especially during the acute phase. While surgical reconstruction is the gold standard treatment for the disease, it requires stability of the disease process and comes with an increased risk of morbidity, evidenced by high rates (65%) of patient dissatisfaction [6]. Thus, the clinical and social consequences of PD illuminate the urgency with which suitable treatments are needed. The goal of this article is to review the current management

This article is part of the Topical Collection on *Female Sexual Dysfunction and Disorders*

✉ Jesse N. Mills
JNMills@mednet.ucla.edu

[1] Division of Andrology, Department of Urology, David Geffen School of Medicine, University of California, 10945 Le Conte Avenue, Ueberroth #3361, Los Angeles, CA 90095, USA

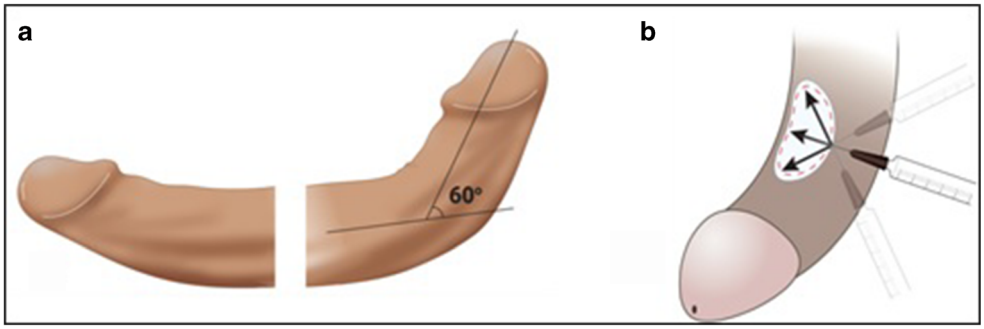

Fig. 1 **a** Normal erect penis without curvature and erect penis with 60° dorsal curvature due to Peyronie's disease. **b** Intralesional CCH injected into PD plaque using "fan" technique

options for PD, focusing on the acute phase of the disease, while acknowledging the variable definitions of the disease course that have been used across different studies.

Defining the Acute Phase

There are two phases that have been recognized in PD: active/acute phase and chronic phase. According to the most recent guidelines by the American Urological Association (AUA), active disease is characterized by dynamic and changing symptoms, with pain or discomfort regardless of erectile function status. Chronic phase is defined as clinically unchanged symptoms for at least 3 months with very little pain [7]. Additionally, the acute phase has been defined by the presence of inflammatory infiltrate within the lesions on the tunica albuginea, whereas those of the stable phase exhibits fibrosis and calcification [8]. The length of time of active phase, however, has been shown to vary across studies and trials and early studies even show no significant association between disease duration and spontaneous improvement in penile bending. This confounds the assignment of defining parameters to acute phase [9]. It is generally accepted that the acute phase can last 12 to 18 months, yet some studies do not use a temporal factor at all in the categorization of acute phase [10•, 11]. Table 1 summarizes the definition of acute phase in the inclusion criteria of various studies, highlighting the variation that can be seen in the literature.

Management with Oral Agents

Ingestable treatments are an alluring option for many patients because of the convenience. However, in examining the published controlled trials, there is no evidence of benefit with the use of colchicine, tamoxifen, vitamin E, potassium aminobenzoate, carnitine, or omega-3 fatty acids [5]. While pentoxifylline and L-arginine have been shown to have beneficial effects in animal model studies, demonstrating scar regression in PD via increasing the levels of nitrous oxide and/or cGMP/cAMP, the literature does not support these as a beneficial therapeutic modality thus far, especially as monotherapeutic agents, and therefore they are not recommended in the International Consultation on Sexual Medicine (ICSM) guidelines [19•, 20]. Additionally, the European Association of Urology (EAU) guidelines recommend against the use of oral vitamin E and tamoxifen with level 2b evidence, and against L-carnitine and pentoxifylline with level 3 evidence [21].

Phosphodiesterase type 5 inhibitors (PDE5Is) have been established as a safe option to treat ED that is often associated with PD, but there is a lack of evidence to show benefit of use of PDE5Is in the treatment of PD-related penile deformity. Thus, their use would not be recommended for this purpose and have not been studied for use in the acute phase of PD [22, 23•]. It is also important to note that as there are no FDA-approved oral therapies for PD, physicians who recommend oral therapy to their patients must inform them that it is an off-label indication.

Topical Management

Verapamil

Topical therapy is an attractive option for patients given its self-directed nature and minimization of systemic adverse effects, but there is a lack of evidence suggesting that agents, such as topical verapamil, are sufficiently able to penetrate transdermally into the tunica albuginea. Topical verapamil has been previously investigated for use in the setting of PD because of its antifibrotic effect on fibroblasts, but because of its lack of penetration as well as the lack of adequate studies to support its use, it is not recommended in PD patients according to ICSM guidelines (grade B, level 3) [24–26].

H-100

The most recent literature evaluating topical therapies has demonstrated that H-100 gel may be a promising novel topical agent. H-100 gel, which combines a natural carrier agent, nicardipine, superoxide dismutase, and emu oil, has been

Table 1 Studies demonstrating varying definitions of acute/active phase PD as mentioned in the inclusion criteria

Author(s)	Study design	*N*	Symptom duration defining acute phase	Pain as a defining criterion	Other criteria (besides curvature)
Gelbard, M. 2012. [12]	Phase II randomized clinical trial	147	≤ 6 months	Not defined	Functional difficulty required (ED or difficulty with intromission)
Gelbard, M. et al. 2013. (IMPRESS I & II) [13]	Phase III randomized placebo-controlled trial	832	≤ 12 months	Not defined	-
Levine, L. et al. 2015. [14]	Phase III open-label clinical trial	347	≤ 12 months	Not defined	-
Zucchi, A. et al. 2016. [15]	Prospective interventional study	65	Not defined	Required	Palpable nodule or plaque required
Twidwell, J. et al. 2016. [16••]	Prospective randomized controlled study	22	< 12 months	Not defined	-
Nguyen, HMT. et al. 2017. [17••]	Retrospective cohort study	162	≤ 12 months	Required	-
Favilla, V. et al. 2017. [10•]	Prospective, randomized trial	201	< 12 months	And/or painful erection	And/or recent change in penile curvature
Martínez-Salamanca, J. et al. 2014. [18]	Prospective, non-randomized, controlled trial	96	< 12 months	Pain at rest or with erection	Progressive penile curvature > 15°

shown to reduce penile curvature and pain and increase penile length in the setting of PD, while maintaining safety [16••]. The prospective, randomized, double-blinded, placebo-controlled pilot study involved 22 patients, all of whom were required to have documented PD of < 12 months duration and were therefore in the acute phase. Compared with the placebo group, the H-100 group experienced a statistically significant reduction in mean curvature (40.8%), as well as a 22.6% increase in penile length, and 85.7% decrease in pain level. Additionally, crossover patients from placebo to H-100 groups also showed significant improvement in all parameters [16••]. As this was a pilot study and the only publication investigating the use of H-100 for PD, larger randomized trials examining efficacy are required before this therapy can be recommended for usage [19•].

Electromotive Drug Administration

As a result of the lack of penetration that was seen in topical therapy, electromotive drug administration (EMDA), or iontophoresis, was developed in an attempt to improve effectiveness. The technique involves the transport of ions through tissue via an electric current in order to electrokinetically direct the medication towards the target lesion. However, the procedure is labor and equipment intensive compared with standard topical application [27]. Initial trials showed promise with the use of various topical drugs using this method in the setting of PD, but subsequent studies continued to demonstrate no benefit of using pharmacologic agents augmented by iontophoresis for the use of PD [28–31]. Additionally, as EMDA is rarely used clinically, there have been no recent studies conducted to further evaluate the efficacy of this therapy for treatment of acute or chronic PD.

Intralesional Injection

Intralesional therapy has the benefit of local drug delivery with high concentrations and has proven to have greater efficacy than topical and oral medications in the treatment of PD. It has been suggested that traumatic disruption of the plaque by the needle might also have a benefit, and with certain injection techniques such as the "fan" technique (Fig. 1b) or percutaneous needle tunneling, procedural morbidity can be minimized while maximizing efficacy [23•, 32•, 33•].

Corticosteroids

Corticosteroids were the first intralesional therapy for PD, employed for their anti-inflammatory effects and initial studies suggesting curvature improvement; however, subsequent studies showed no significant difference between corticosteroid and placebo groups [34–36]. Furthermore, because of the adverse systemic effects associated with corticosteroid use, such as tissue atrophy and wound infection, along with its limited efficacy, the AUA and the EAU do not recommend its use for the treatment of PD [7, 21].

Table 2 Comparison of CCH treatment protocols and their efficacy for PD

	Dose of CCH	Maximum number of cycles	Cycle duration (week)	Total duration of treatment (week)	Curvature improvement (from baseline)
Standard protocol	0.58 mg	4	6	24	34% [13]
Shortened modified protocol	0.9 mg	3	4	12	31.4% [46•]

Collagenase *Clostridium histolyticum*

To date, the only medication Food and Drug Administration (FDA) approved for the treatment of PD is Collagenase *Clostridium histolyticum* (CCH), which works to cleave irregular amalgamations of collagen. It is administered as injections directly into a plaque at multiple clinic appointments, followed by several weeks of mechanical stretching of the penis (Fig. 1b) [13, 37•, 38]. Previously used to treat Dupuytren's contracture, CCH consists of purified enzymes produced by the bacterium *Clostridium histolyticum*, cleaving types I and III collagen, the most abundant types found in PD plaques [19•, 39].

Initial randomized, placebo-controlled, double-blinded trials demonstrated statistically significant improvement in penile curvature while maintaining safety, thereby prompting larger studies [40, 41]. IMPRESS I and II, two large randomized double-blinded, placebo-controlled phase II trials, confirmed the efficacy of CCH with a low complication rate. In these trials, the subjects received up to 8 injections of 0.58 mg CCH separated into 4 cycles with 2 injections each, separated by 24 to 72 h, a regimen that ultimately showed a statistically significant 34% improvement in curvature compared with placebo (18.2%), and became the standard protocol [13]. Subsequent studies continued to show similar results, confirming the safety and efficacy of CCH for the treatment of PD [14, 38, 42•, 43]. In addition, recent studies have shown that the standard protocol of CCH is both safe and effective specifically during the acute phase of PD, a result that still needs confirmation by large multi-institutional studies [44••].

Besides the efficacy and safety that has been consistently reported with the use of CCH, the cost of the drug therapy is considerable, with one cost analysis totaling treatment of severe disease to US$26,375 (considerably more expensive than other therapies), an aspect of treatment that cannot be ignored [45]. Some clinicians are beginning to propose new modified protocols of CCH treatment administration aiming at lowering the cost to patients while maintaining efficacy [46•]. Table 2 draws a comparison between the standard protocol and the shortened modified protocol, though these protocols have yet to be directly compared in studies examining the acute phase of PD. Additionally, given that CCH treatment for PD is approved specifically for dorsal or dorsolateral curves between 30° and 90°, ventral plaques have not been widely studied due to previous concerns of urethral injury during penile modeling [47]. However, recent studies suggest that men with ventral PD may be effectively treated with CCH, with similar adverse events to treatment of other curvature directions [48••].

Intralesional Verapamil

Similar to the mechanism of action of topical verapamil, intralesional verapamil has been used for PD based on evidence showing its interference with fibroblast cellular proliferation [24, 49]. Multiple randomized studies have evaluated intralesional verapamil for the treatment of PD; however, results are mixed [50–55]. Recent studies have compared it against various therapies, including tadalafil, hyaluronic acid (HA), and thiocolchicine [10•, 56, 57]. In the trial comparing intralesional verapamil with tadalafil, there was no statistically significant improvement in curvature observed with verapamil, a result also seen in a prospective, randomized, double-blinded study comparing verapamil with HA. This trial did, however, show a greater efficacy of HA regarding penile curvature and patient satisfaction [10•, 56]. Intralesional thiocolchicine had similar curvature improvements to that of verapamil in a prospective, randomized study, but the study was limited due to a small sample size ($N = 25$) [57]. Overall, intralesional verapamil has been shown to be modestly beneficial in the treatment of PD in the acute phase.

Hyaluronic Acid

Intralesional HA functions to decrease inflammatory cytokines and, as mentioned, has shown efficacy in the treatment of PD, with improvements in penile curvature and patient satisfaction [10•]. Studies have also shown similar results with HA use specifically during the acute phase of PD, yet further prospective, randomized controlled trials are required in order for intralesional HA to be regularly recommended [58].

Plasma-Rich Platelets + Hyaluronic Acid

Platelet-derived therapies are a growing interest in multiple medical and surgical specialties and one of the most well-described platelet-based therapies is autologous plasma-rich platelets (PRP) [59]. Initial small studies suggest that the anti-inflammatory and wound-healing properties of platelets are safe and efficacious in the treatment of various urologic

conditions such as ED, PD, and stress urinary incontinence [60•]. However, this is controversial and hotly debated. Currently, the Sexual Medicine Society of North America (SMSNA) positions against these therapies as nothing more than experimental.

PRP is derived from the centrifugation of whole blood with a separator gel to remove the red and white blood cells; this results in a supernatant that has a greater-than-fourfold increase in platelets and other plasma proteins. This is the concentrate that is then injected; studies are also evaluating strategies that focus on maximizing efficacy of drug delivery by creating a fibrin matrix to prevent extravasation [61, 62].

A recent study evaluated the use of a combination of PRP and HA for the treatment of PD. Ninety patients were injected with 8 ml of the combination 4 times over the course of 2 months. The study found a statistically significant improvement in penile curvature and thickening of the tunica albuginea, with 70% of patients reporting the treatment as positive [63•]. With confirmation by larger studies, this treatment may prove effective as another treatment for PD. It is critical to point out that this treatment will likely never approach FDA scrutiny and therefore is still considered controversial.

Interferon-α2b

Interferon-α2b (IFNα2b) is an immunomodulator approved for utilization in various malignancies and infections and functions by inhibiting cellular proliferation. It has been shown to decrease fibroblast proliferation and collagen production in PD plaques in vitro and was first used to treat PD in the 1990s [64–66]. Evidence has shown that intralesional IFNα2b leads to significant improvement in penile curvature and has even shown this improvement when applied to ventral deformities, for which the FDA has contraindicated the use of CCH [65, 67, 68]. While IFNα2b is associated with self-limiting flu-like symptoms, it has a good safety profile in general and can produce clinically meaningful results to patients, recognized as one of the superior agents (along with CCH) regarding outcomes of penile curvature; however, it still remains off-label according to the FDA and AUA guidelines [7, 69•].

Mycophenolate mofetil

Mycophenolate mofetil (MMF) is an immunosuppressive drug used to prevent organ rejection after transplantation and has shown some efficacy in preventing the fibrotic complications of autoimmune disease such as systemic sclerosis or graft-versus-host disease [70]. It has been proposed that MMF may have a role in altering fibroblast function via altering collagen production, extracellular matrix contraction, and cell migration [70]. Given this property, one study evaluating the role of MMF in a murine PD model suggests that the drug acts as a regenerating antifibrotic agent that may be useful for translation to human PD [71••]. No current human trials exist to develop this therapy into a viable option in the near future.

Shockwave Therapy

Local extracorporeal shockwave therapy (ESWT) is hypothesized to act in the setting of PD by two mechanisms. First, it is thought that the shockwaves directly disrupt the PD plaque, leading to lysis by way of an inflammatory reaction; second, the shockwaves are thought to promote angiogenesis around the plaque, resulting in plaque resorption [72].

Most of the published literature thus far has failed to show any significant benefit of ESWT in the treatment of PD-related penile curvature [73–76]. Some studies demonstrated a statistically significant improvement in curvature; however, the degree of change was minimal and likely clinically meaningless [74]. Other studies suggest that ESWT may be beneficial in the management of PD for refractory penile pain and plaque size reduction, but given that pain usually resolves spontaneously over time in PD, ESWT may be nothing more than a financial burden [77]. ESWT is not recommended for use in PD at this time; however, more recent studies showing reduced plaque size, increased penile length, and clinically and statistically significant improvement in curvature specifically in acute phase PD suggest that ESWT may be entered into consideration in the future [78•]. Again, physicians who offer ESWT to patients should strive to inform them that there are no validated, reproducible protocols for PD.

External Mechanical Therapy

External mechanical therapy can be divided into two categories: vacuum therapy and penile traction therapy. Vacuum therapy utilizes external physical force in an attempt to reorder collagen and promote remodeling within the scar tissue. A series of 31 patients applied vacuum therapy for 10 min per session twice daily for 12 weeks. Authors reported a statistically significant improvement in length and curvature, with 21 men seeing improvement, 7 men seeing no change, and 3 men experiencing worsened curvature [79]. Importantly, this study contained men in the acute phase, with the average duration of symptoms being 9.9 months and ranging from 2 to 23 months [79]. However, since the men in the acute phase were not separated for analysis, it may be that these patients were over or underrepresented in the 21 men seeing improvement. A pilot study evaluating the role of vacuum therapy in addition to a shortened and modified CCH injection protocol found all patients who received CCH in addition to vacuum therapy had an average of roughly 40% improvement in curvature [80].

Vacuum therapy was applied twice daily and involved repeating 40-s applications 5 times. The authors concluded that vacuum therapy with or without additional modeling is a viable adjunct to CCH therapy, but the limited sample size of this study requires verification [80]. The inclusion criteria of this study required stable PD symptoms and therefore excluded men in the acute phase.

Penile traction therapy has been investigated with or without accompanying CCH in the treatment of PD [18, 81, 82, 83•, 84, 85]. Certain studies have showed limited benefits of penile traction therapies; however, they have been limited by patient self-discontinuation of therapy due to practical considerations [81, 82]. A larger prospective study found that among the 113 patients who completed both CCH and daily traction therapy, traction therapy with the RestoreX device gained an additional 71% in curvature improvement over CCH alone [83•]. Importantly, only 113 of 287 total patients completed therapy. This highlights the practical burden of traction and CCH therapy [83•]. A pilot study of 19 patients showed limited improvement in penile length, but increased satisfaction in men with traction therapy in men with curvatures less than 50° [84]. An earlier pilot study of 10 men found curvature reductions of 33% with traction therapy that required application 2 to 8 h a day for 6 months [85]. The prolonged daily use and the limited sample size may be factors contributing to the reported efficacy, which has not been reproduced by subsequent studies. Finally, a study evaluating the role of traction therapy specifically in the acute phase found that men experienced a 20° average curvature reduction and 42% of men regained the ability to have penetrative intercourse [18]. These impressive results may be due to the daily 6 h of traction therapy for at least 6 months; however, men in the acute phase may see similar results with extensive traction therapy.

Surgical Management

Surgical therapies can be divided into two categories: reconstructive surgery and penile prosthesis implantation. Both require that patients are not in the acute phase of PD [86]. Reconstructive operations generally fall into two categories: shortening of the convex side or lengthening of the concave side [86]. The Nesbit and Yachia procedures fall into the former and while correcting curvature in a vast majority of patients, they are prone to penile shortening and sensory changes [87–95]. Additionally, they can result in post-operative erectile dysfunction. A less technically demanding option for shortening the concave surface is penile plication, which exhibits slightly lower rates of curvature correction and similar rates of shortening, ED, and sensory changes [96–102]. The other category of operations which rely on lengthening the concave surface of the PD penis involves plaque incision and grafting. Grafting is more appropriate for patients with larger and more complex deformities and can utilize a variety of autologous and cadaveric tissues [86]. Incision-and-grafting is a lengthening procedure and thus corrects curvature effectively with minimal penile shortening experienced in the literature [102–116]. However, this surgery also results in significant rates of post-operative ED and penile numbness [102–117]. In order to optimize patient selection and satisfaction, men must be counseled to not expect a result that resembles their penis before PD as the invasive surgical technique results in permanent aesthetic changes. Table 3 provides a comparison of the post-operative complication rates between the various surgical techniques, based on the literature.

The other category of surgical management is penile prosthesis placement, which is more appropriate in men with severe ED in addition to PD, both of which are not amenable to conservative therapies [86]. Compared with a traditional prosthesis placement, the operative technique often involves additional steps specifically aimed at reducing curvature in the patient with PD. As a result, efficacy is somewhat lower than the reconstructive options; however, ED is simultaneously corrected [118–125]. Additional grafts can be placed in order to correct curvature in addition to the prosthesis itself. Finally, complications of the prosthesis itself, such as infection, erosion, and explant, are possible with prosthesis placement [86].

Conclusion

A variety of treatments have been proposed for PD, the majority of which focus on the chronic phase of the disease. More recent literature, however, has focused on the acute phase of the disease. Oral monotherapy for PD has shown minimal

Table 3 Comparison of post-operative complication rates between various surgical techniques [87–125]

Surgical procedure	Subjective penile shortening to any degree	Sensory changes	Erectile dysfunction
Nesbit procedure	17.4–100%	3.8–21.4%	0–23%
Yachia procedure	7–67%	2–31%	4–7%
Plication-only procedure	8.3–90%	3.5–75%	3–36%
Incision-and-grafting	0–59%	8–20%	0–25%

efficacy in general and is not currently recommended for treatment of acute phase PD. Topical therapies have also shown to be ineffective; however, novel therapies are on the horizon and may show promise. External mechanical therapies have shown clinically meaningful changes but require much dedication and time from the patient in order to be successful.

As the only FDA-approved medication for PD, CCH is a reasonable alternative to surgery and has proven to be effective in stable PD. It has also been suggested that CCH has similar efficacy during the acute phase of the disease, a finding that will likely continue to be evaluated in future studies. Other intralesional therapies are promising but still require additional large studies to confirm efficacy in order for them to be considered for regular recommendation.

The most advantageous regimen for the treatment of acute phase PD likely incorporates multiple modalities, and further research along with the illumination of novel therapies will increase the amount of options. At this time, however, surgery remains the gold standard for the treatment of PD.

Compliance with Ethical Standards

Conflict of Interest Dr. Jesse Mills reports a grant and personal fees from Boston Scientific as a consultant and speaker, and a grant and personal fees from Endo Pharmaceuticals, outside of submitted work. Dr. Eleswarapu reports personal fees from Metuchen Pharmaceuticals as consultant and speaker, outside of submitted work. Dr. Amighi, Dr. Walker, and Dr. Steven Mills declare no conflicts of interest.

Research involving human participants and/or animals This article does not contain any studies with human or animal subjects performed by the author.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Dibenedetti DB, Nguyen D, Zografos L, Ziemiecki R, Zhou X. A population-based study of Peyronie's disease: prevalence and treatment patterns in the United States. Adv Urol. 2011;2011:282503. https://doi.org/10.1155/2011/282503.
2. Ostrowski KA, Gannon JR, Walsh TJ. A review of the epidemiology and treatment of Peyronie's disease. Res Rep Urol. 2016;8:61–70. https://doi.org/10.2147/RRU.S65620.
3. Nelson CJ, Diblasio C, Kendirci M, Hellstrom W, Guhring P, Mulhall JP. The chronology of depression and distress in men with Peyronie's disease. J Sex Med. 2008;5(8):1985–90. https://doi.org/10.1111/j.1743-6109.2008.00895.x.
4. Smith JF, Walsh TJ, Conti SL, Turek P, Lue T. Risk factors for emotional and relationship problems in Peyronie's disease. J Sex Med. 2008;5(9):2179–84. https://doi.org/10.1111/j.1743-6109.2008.00949.x.
5. Levine LA. Peyronie's disease: contemporary review of non-surgical treatment. Transl Androl Urol. 2013;2(1):39–44. https://doi.org/10.3978/j.issn.2223-4683.2013.01.01.
6. Chung E, Clendinning E, Lessard L, Brock G. Five-year follow-up of Peyronie's graft surgery: outcomes and patient satisfaction. J Sex Med. 2011;8(2):594–600. https://doi.org/10.1111/j.1743-6109.2010.02102.x.
7. Nehra A, Alterowitz R, Culkin DJ, Faraday MM, Hakim LS, Heidelbaugh JJ, et al. Peyronie's disease: AUA guideline. J Urol. 2015;194(3):745–53. https://doi.org/10.1016/j.juro.2015.05.098.
8. Tefekli A, Kandirali E, Erol H, Alp T, Koksal T, Kadioglu A. Peyronie's disease in men under age 40: characteristics and outcome. Int J Impot Res. 2001;13(1):18–23. https://doi.org/10.1038/sj.ijir.3900635.
9. Gelbard MK, Dorey F, James K. The natural history of Peyronie's disease. J Urol. 1990;144(6):1376–9.
10. • Favilla V, Russo GI, Zucchi A, Siracusa G, Privitera S, Cimino S, et al. Evaluation of intralesional injection of hyaluronic acid compared with verapamil in Peyronie's disease: preliminary results from a prospective, double-blinded, randomized study. Andrology. 2017;5(4):771–5. https://doi.org/10.1111/andr.12368 **This prospective, double-blinded, randomized study described improvements in penile curvature and patient satisfaction with the use of intralesional HA, and is thus an important study in the evaluation of HA for PD therapy.**
11. Mulhall JP, Schiff J, Guhring P. An analysis of the natural history of Peyronie's disease. J Urol. 2006;175(6):2115–8; discussion 8. https://doi.org/10.1016/S0022-5347(06)00270-9.
12. Gelbard M, Lipshultz LI, Tursi J, Smith T, Kaufman G, Levine LA. Phase 2b study of the clinical efficacy and safety of collagenase Clostridium histolyticum in patients with Peyronie disease. J Urol. 2012;187(6):2268–74. https://doi.org/10.1016/j.juro.2012.01.032.
13. Gelbard M, Goldstein I, Hellstrom WJ, McMahon CG, Smith T, Tursi J, et al. Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of peyronie disease in 2 large double-blind, randomized, placebo controlled phase 3 studies. J Urol. 2013;190(1):199–207. https://doi.org/10.1016/j.juro.2013.01.087.
14. Levine LA, Cuzin B, Mark S, Gelbard MK, Jones NA, Liu G, et al. Clinical safety and effectiveness of collagenase clostridium histolyticum injection in patients with Peyronie's disease: a phase 3 open-label study. J Sex Med. 2015;12(1):248–58. https://doi.org/10.1111/jsm.12731.
15. Zucchi A, Costantini E, Cai T, Cavallini G, Liguori G, Favilla V, et al. Intralesional injection of hyaluronic acid in patients affected with Peyronie's disease: preliminary results from a prospective, multicenter, pilot study. Sex Med. 2016;4(2):e83–8. https://doi.org/10.1016/j.esxm.2016.01.002.
16. •• Twidwell J, Levine L. Topical treatment for acute phase Peyronie's disease utilizing a new gel, H-100: a randomized, prospective, placebo-controlled pilot study. Int J Impot Res. 2016;28(2):41–5. https://doi.org/10.1038/ijir.2015.22 **This randomized, prospective, placebo-controlled pilot study evaluated the use of a potentially novel topical therapy for PD, H-100 gel, with promising results.**
17. •• Nguyen HMT, Anaissie J, DeLay KJ, Yafi FA, Sikka SC, Hellstrom WJG. Safety and efficacy of collagenase Clostridium histolyticum in the treatment of acute-phase Peyronie's disease. J Sex Med. 2017;14(10):1220–5. https://doi.org/10.1016/j.jsxm.2017.08.008 **This study suggests that CCH use during the acute phase can be effective and safe, an important result for future research and management guidelines.**
18. Martinez-Salamanca JI, Egui A, Moncada I, Minaya J, Ballesteros CM, Del Portillo L, et al. Acute phase Peyronie's disease

management with traction device: a nonrandomized prospective controlled trial with ultrasound correlation. J Sex Med. 2014;11(2):506–15. https://doi.org/10.1111/jsm.12400.

19.• Randhawa K, Shukla CJ. Non-invasive treatment in the management of Peyronie's disease. Ther Adv Urol. 2019;11:1756287218823671. https://doi.org/10.1177/1756287218823671 **This review article provides a recent overview of PD management options without focus on a particular phase of PD.**

20. Valente EG, Vernet D, Ferrini MG, Qian A, Rajfer J, Gonzalez-Cadavid NF. L-arginine and phosphodiesterase (PDE) inhibitors counteract fibrosis in the Peyronie's fibrotic plaque and related fibroblast cultures. Nitric Oxide. 2003;9(4):229–44. https://doi.org/10.1016/j.niox.2003.12.002.

21. Hatzimouratidis K, Eardley I, Giuliano F, Hatzichristou D, Moncada I, Salonia A, et al. EAU guidelines on penile curvature. Eur Urol. 2012;62(3):543–52. https://doi.org/10.1016/j.eururo.2012.05.040.

22. Levine LA, Latchamsetty KC. Treatment of erectile dysfunction in patients with Peyronie's disease using sildenafil citrate. Int J Impot Res. 2002;14(6):478–82. https://doi.org/10.1038/sj.ijir.3900912.

23.• Tsambarlis P, Levine LA. Nonsurgical management of Peyronie's disease. Nat Rev Urol. 2019;16(3):172–86. https://doi.org/10.1038/s41585-018-0117-7 **This review article provides a recent overview of PD management options without focus on a particular phase of PD.**

24. Aggeler J, Frisch SM, Werb Z. Changes in cell shape correlate with collagenase gene expression in rabbit synovial fibroblasts. J Cell Biol. 1984;98(5):1662–71. https://doi.org/10.1083/jcb.98.5.1662.

25. Chung E, Ralph D, Kagioglu A, Garaffa G, Shamsodini A, Bivalacqua T, et al. Evidence-based management guidelines on Peyronie's disease. J Sex Med. 2016;13(6):905–23. https://doi.org/10.1016/j.jsxm.2016.04.062.

26. Martin DJ, Badwan K, Parker M, Mulhall JP. Transdermal application of verapamil gel to the penile shaft fails to infiltrate the tunica albuginea. J Urol. 2002;168(6):2483–5. https://doi.org/10.1097/01.ju.0000031440.26763.da.

27. Levine LA, Estrada CR, Shou W, Cole A. Tunica albuginea tissue analysis after electromotive drug administration. J Urol. 2003;169(5):1775–8. https://doi.org/10.1097/01.ju.0000056153.47716.d0.

28. Greenfield JM, Shah SJ, Levine LA. Verapamil versus saline in electromotive drug administration for Peyronie's disease: a double-blind, placebo controlled trial. J Urol. 2007;177(3):972–5. https://doi.org/10.1016/j.juro.2006.10.065.

29. Mehrsai AR, Namdari F, Salavati A, Dehghani S, Allameh F, Pourmand G. Comparison of transdermal electromotive administration of verapamil and dexamethasone versus intra-lesional injection for Peyronie's disease. Andrology. 2013;1(1):129–32. https://doi.org/10.1111/j.2047-2927.2012.00018.x.

30. Montorsi F, Salonia A, Guazzoni G, Barbieri L, Colombo R, Brausi M, et al. Transdermal electromotive multi-drug administration for Peyronie's disease: preliminary results. J Androl. 2000;21(1):85–90.

31. Riedl CR, Plas E, Engelhardt P, Daha K, Pfluger H. Iontophoresis for treatment of Peyronie's disease. J Urol. 2000;163(1):95–9.

32.• Amighi A, Mills SA, Eleswarapu SV, Regets KV, Mendhiratta N, Mills JN. A modified technique for intralesional injection of collagenase Clostridium histolyticum for Peyronie's disease results in reduced procedural morbidity using a standardized hematoma classification rubric. World J Urol. 2019. https://doi.org/10.1007/s00345-019-02812-9 **This article proposes a modified technique for intralesional injection of CCH, showing reduced procedural morbidity.**

33.• Fernandez-Pascual E, Gonzalez-Garcia FJ, Angulo J, Cerezo E, Quintana LM, Turo J, et al. Optimizing collagenase Clostridium histolyticum therapy for Peyronie's disease using a novel approach with percutaneous needle tunnelling. BJU Int. 2019. https://doi.org/10.1111/bju.14784 **This article describes a specific technique for intralesional injection of CCH with improved outcomes.**

34. Cipollone G, Nicolai M, Mastroprimiano G, Iantorno R, Longeri D, Tenaglia R. Betamethasone versus placebo in Peyronie's disease. Arch Ital Urol Androl. 1998;70(4):165–8.

35. Desanctis PN, Furey CA Jr. Steroid injection therapy for Peyronie's disease: a 10-year summary and review of 38 cases. J Urol. 1967;97(1):114–6. https://doi.org/10.1016/s0022-5347(17)62993-8.

36. Winter CC, Khanna R. Peyronie's disease: results with dermo-jet injection of dexamethasone. J Urol. 1975;114(6):898–900. https://doi.org/10.1016/s0022-5347(17)67169-6.

37.• Haney NM, Kohn TP, Nichols PE, Jg Hellstrom W. The effect of adjunct mechanical traction on penile length in men undergoing primary treatment for Peyronie's disease: a systematic review and meta-analysis. Urology. 2018;122:110–5. https://doi.org/10.1016/j.urology.2018.07.039 **This meta-analysis explored the use of penile traction therapy in conjunction with PD treatment. As mechanical traction therapy is often used in conduction with CCH therapy in clinical practice, this article is important in evaluating the efficacy of such.**

38. Lipshultz LI, Goldstein I, Seftel AD, Kaufman GJ, Smith TM, Tursi JP, et al. Clinical efficacy of collagenase Clostridium histolyticum in the treatment of Peyronie's disease by subgroup: results from two large, double-blind, randomized, placebo-controlled, phase III studies. BJU Int. 2015;116(4):650–6. https://doi.org/10.1111/bju.13096.

39. Brazzelli M, Cruickshank M, Tassie E, McNamee P, Robertson C, Elders A, et al. Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation. Health Technol Assess. 2015;19(90):1–202. https://doi.org/10.3310/hta19900.

40. Gelbard MK, James K, Riach P, Dorey F. Collagenase versus placebo in the treatment of Peyronie's disease: a double-blind study. J Urol. 1993;149(1):56–8.

41. Jordan GH. The use of intralesional clostridial collagenase injection therapy for Peyronie's disease: a prospective, single-center, non-placebo-controlled study. J Sex Med. 2008;5(1):180–7. https://doi.org/10.1111/j.1743-6109.2007.00651.x.

42.• Abdel Raheem A, Capece M, Kalejaiye O, Abdel-Raheem T, Falcone M, Johnson M, et al. Safety and effectiveness of collagenase clostridium histolyticum in the treatment of Peyronie's disease using a new modified shortened protocol. BJU Int. 2017;120(5):717–23. https://doi.org/10.1111/bju.13932 **This prospective study evaluated a shortened protocol for the intralesional injection of CCH, showing the method to be both efficacious and cost efficient. When considering the potentially high cost of CCH therapy, it is important that this study demonstrated a more cost-efficient protocol.**

43. Ziegelmann MJ, Viers BR, McAlvany KL, Bailey GC, Savage JB, Trost LW. Restoration of penile function and patient satisfaction with intralesional collagenase Clostridium histolyticum injection for Peyronie's disease. J Urol. 2016;195(4 Pt 1):1051–6. https://doi.org/10.1016/j.juro.2015.10.065.

44.•• El-Khatib FM, Towe M, Yafi FA. Management of Peyronie's disease with collagenase Clostridium histolyticum in the acute phase. World J Urol. 2019. https://doi.org/10.1007/s00345-019-02791-x **This review article summarized the use of intralesional injection of CCH in the acute phase of PD, concluding that there may be comparable efficacy as to treatment of chronic phase.**

45. Cordon BH, Hofer MD, Hutchinson RC, Broderick GA, Lotan Y, Morey AF. Superior cost effectiveness of penile plication vs intralesional collagenase injection for treatment of Peyronie's disease deformities. Urol Pract. 2017;(4):118–25. https://doi.org/10.1016/j.urpr.2016.04.005.
46.• Abdel Raheem A, Johnson M, Ralph D, Garaffa G. Collagenase clostridium histolyticum: a novel medical treatment for Peyronie's disease. Minerva Urol Nefrol. 2018;70(4):380–5. https://doi.org/10.23736/S0393-2249.18.03118-1 **This article suggests a new modified protocol for the intralesional injection of CCH that reduces the cost and inconvenience to patients while maintaining efficacy. This will potentially allow more men to benefit and will reduce the number of men undergoing surgical correction for their PD.**
47. Gabrielson AT, Spitz JT, Hellstrom WJG. Collagenase Clostridium histolyticum in the treatment of urologic disease: current and future impact. Sex Med Rev. 2018;6(1):143–56. https://doi.org/10.1016/j.sxmr.2017.03.005.
48.•• Alom M, Meng Y, Sharma KL, Savage J, Kohler T, Trost L. Safety and efficacy of collagenase Clostridium histolyticum in Peyronie's disease men with ventral curvatures. Urology. 2019;129:119–25. https://doi.org/10.1016/j.urology.2019.01.055 **This prospective study explored the use of intralesional injection of CCH in ventral curvatures. This study is important as CCH has previously been studied widely for dorsal curvatures only.**
49. Roth M, Eickelberg O, Kohler E, Erne P, Block LH. Ca2+ channel blockers modulate metabolism of collagens within the extracellular matrix. Proc Natl Acad Sci U S A. 1996;93(11):5478–82. https://doi.org/10.1073/pnas.93.11.5478.
50. Bennett NE, Guhring P, Mulhall JP. Intralesional verapamil prevents the progression of Peyronie's disease. Urology. 2007;69(6):1181–4. https://doi.org/10.1016/j.urology.2007.02.042.
51. Levine LA. Treatment of Peyronie's disease with intralesional verapamil injection. J Urol. 1997;158(4):1395–9.
52. Levine LA, Goldman KE, Greenfield JM. Experience with intraplaque injection of verapamil for Peyronie's disease. J Urol. 2002;168(2):621–5; discussion 5-6. https://doi.org/10.1016/s0022-5347(05)64691-5.
53. Levine LA, Merrick PF, Lee RC. Intralesional verapamil injection for the treatment of Peyronie's disease. J Urol. 1994;151(6):1522–4. https://doi.org/10.1016/s0022-5347(17)35291-6.
54. Rehman J, Benet A, Melman A. Use of intralesional verapamil to dissolve Peyronie's disease plaque: a long-term single-blind study. Urology. 1998;51(4):620–6.
55. Shirazi M, Haghpanah AR, Badiee M, Afrasiabi MA, Haghpanah S. Effect of intralesional verapamil for treatment of Peyronie's disease: a randomized single-blind, placebo-controlled study. Int Urol Nephrol. 2009;41(3):467–71. https://doi.org/10.1007/s11255-009-9522-4.
56. Dell'Atti L. Tadalafil once daily and intralesional verapamil injection: a new therapeutic direction in Peyronie's disease. Urol Ann. 2015;7(3):345–9. https://doi.org/10.4103/0974-7796.152048.
57. Toscano L Jr, Rezende MV, Mello LF, Paulillo D, Glina S. A prospective, randomized, single - blind study comparing intraplaque injection of thiocolchicine and verapamil in Peyronie's disease: a pilot study. Int Braz J Urol. 2016;42(5):1005–9. https://doi.org/10.1590/S1677-5538.IBJU.2015.0598.
58. Gennaro R, Barletta D, Paulis G. Intralesional hyaluronic acid: an innovative treatment for Peyronie's disease. Int Urol Nephrol. 2015;47(10):1595–602. https://doi.org/10.1007/s11255-015-1074-1.
59. Xie X, Zhang C, Tuan RS. Biology of platelet-rich plasma and its clinical application in cartilage repair. Arthritis Res Ther. 2014;16(1):204. https://doi.org/10.1186/ar4493.
60.• Matz EL, Pearlman AM, Terlecki RP. Safety and feasibility of platelet rich fibrin matrix injections for treatment of common urologic conditions. Investig Clin Urol. 2018;59(1):61–5. https://doi.org/10.4111/icu.2018.59.1.61 **This article reports that the delivery of platelet-rich plasma via a platelet-rich fibrin matrix is safe and feasible for the treatment of ED, PD, and female SUI. This potentially opens doors for studies to evaluate efficacy of this therapy for PD.**
61. Gigante A, Del Torto M, Manzotti S, Cianforlini M, Busilacchi A, Davidson PA, et al. Platelet rich fibrin matrix effects on skeletal muscle lesions: an experimental study. J Biol Regul Homeost Agents. 2012;26(3):475–84.
62. Sampson S, Gerhardt M, Mandelbaum B. Platelet rich plasma injection grafts for musculoskeletal injuries: a review. Curr Rev Musculoskelet Med. 2008;1(3-4):165–74. https://doi.org/10.1007/s12178-008-9032-5.
63.• Virag R, Sussman H, Lambion S, de Fourmestraux V. Evaluation of the benefit of using a combination of autologous platelet rich-plasma and hyaluronic acid for the treatment of Peyronie's disease. Sex Health Issues. 2017;1:1–8. https://doi.org/10.15761/SHI.1000102 **This small study explored the use of a combination of PRP and HA in the treatment of PD with positive results, potentially leading to larger studies of this novel therapy.**
64. Duncan MR, Berman B, Nseyo UO. Regulation of the proliferation and biosynthetic activities of cultured human Peyronie's disease fibroblasts by interferons-alpha, -beta and -gamma. Scand J Urol Nephrol. 1991;25(2):89–94. https://doi.org/10.3109/00365599109024539.
65. Russell S, Steers W, McVary KT. Systematic evidence-based analysis of plaque injection therapy for Peyronie's disease. Eur Urol. 2007;51(3):640–7. https://doi.org/10.1016/j.eururo.2006.10.042.
66. Wegner HE, Andresen R, Knipsel HH, Miller K. Treatment of Peyronie's disease with local interferon-alpha 2b. Eur Urol. 1995;28(3):236–40.
67. Chong W, Tan RB. Injectable therapy for Peyronie's disease. Transl Androl Urol. 2016;5(3):310–7. https://doi.org/10.21037/tau.2016.03.15.
68. Hellstrom WJ, Kendirci M, Matern R, Cockerham Y, Myers L, Sikka SC, et al. Single-blind, multicenter, placebo controlled, parallel study to assess the safety and efficacy of intralesional interferon alpha-2B for minimally invasive treatment for Peyronie's disease. J Urol. 2006;176(1):394–8. https://doi.org/10.1016/S0022-5347(06)00517-9.
69.• Russo GI, Cacciamani G, Cocci A, Kessler TM, Morgia G, Serefoglu EC, et al. Comparative effectiveness of intralesional therapy for Peyronie's disease in controlled clinical studies: a systematic review and network meta-analysis. J Sex Med. 2019;16(2):289–99. https://doi.org/10.1016/j.jsxm.2018.12.011 **This systematic review and meta-analysis focuses on the current intralesional therapies for PD, providing evidence of the efficacy between different intralesional therapies.**
70. Roos N, Poulalhon N, Farge D, Madelaine I, Mauviel A, Verrecchia F. In vitro evidence for a direct antifibrotic role of the immunosuppressive drug mycophenolate mofetil. J Pharmacol Exp Ther. 2007;321(2):583–9. https://doi.org/10.1124/jpet.106.117051.
71.•• Antoniassi T, Junior FNF, Spessoto LCF, Guerra LH, Campos SS, Taboga S. Anti-fibrotic effect of mycophenolate mofetil on Peyronie's disease experimentally induced with TGF-beta. Int J Impot Res. 2019. https://doi.org/10.1038/s41443-019-0138-7 **This study evaluates the role of MMF in a murine PD model and suggests that the drug acts as a regenerating anti-fibrotic agent that may be useful for translation to human PD. This proposes a potential novel therapy for PD.**
72. Levine LA. Review of current nonsurgical management of Peyronie's disease. Int J Impot Res. 2003;15(Suppl 5):S113–20. https://doi.org/10.1038/sj.ijir.3901084.

73. Hauck EW, Hauptmann A, Bschleipfer T, Schmelz HU, Altinkilic BM, Weidner W. Questionable efficacy of extracorporeal shock wave therapy for Peyronie's disease: results of a prospective approach. J Urol. 2004;171(1):296–9. https://doi.org/10.1097/01.ju.0000099891.68488.4e.
74. Palmieri A, Imbimbo C, Longo N, Fusco F, Verze P, Mangiapia F, et al. A first prospective, randomized, double-blind, placebo-controlled clinical trial evaluating extracorporeal shock wave therapy for the treatment of Peyronie's disease. Eur Urol. 2009;56(2):363–9. https://doi.org/10.1016/j.eururo.2009.05.012.
75. Srirangam SJ, Manikandan R, Hussain J, Collins GN, O'Reilly PH. Long-term results of extracorporeal shockwave therapy for Peyronie's disease. J Endourol. 2006;20(11):880–4. https://doi.org/10.1089/end.2006.20.880.
76. Strebel RT, Suter S, Sautter T, Hauri D. Extracorporeal shockwave therapy for Peyronie's disease does not correct penile deformity. Int J Impot Res. 2004;16(5):448–51. https://doi.org/10.1038/sj.ijir.3901192.
77. Krieger JR, Rizk PJ, Kohn TP, Pastuszak A. Shockwave therapy in the treatment of Peyronie's disease. Sex Med Rev. 2019. https://doi.org/10.1016/j.sxmr.2019.02.001.
78.• di Mauro M, Russo GI, Della Camera PA, di Maida F, Cito G, Mondaini N, et al. Extracorporeal shock wave therapy in Peyronie's disease: clinical efficacy and safety from a single-arm observational study. World J Mens Health. 2019. https://doi.org/10.5534/wjmh.180100 **As ESWT is currently not recommended for use for treatment of PD, this study showed positive, statistically significant results with the use of ESWT.**
79. Raheem AA, Garaffa G, Raheem TA, Dixon M, Kayes A, Christopher N, et al. The role of vacuum pump therapy to mechanically straighten the penis in Peyronie's disease. BJU Int. 2010;106(8):1178–80. https://doi.org/10.1111/j.1464-410X.2010.09365.x.
80. Ralph DJ, Abdel Raheem A, Liu G. Treatment of Peyronie's disease with collagenase Clostridium histolyticum and vacuum therapy: a randomized, open-label pilot study. J Sex Med. 2017;14(11):1430–7. https://doi.org/10.1016/j.jsxm.2017.08.015.
81. Ziegelmann MJ, Viers BR, Montgomery BD, Avant RA, Savage JB, Trost LW. Clinical experience with penile traction therapy among men undergoing collagenase Clostridium histolyticum for Peyronie disease. Urology. 2017;104:102–9. https://doi.org/10.1016/j.urology.2017.01.054.
82. Yafi FA, Pinsky MR, Stewart C, Sangkum P, Ates E, Trost LW, et al. The effect of duration of penile traction therapy in patients undergoing intralesional injection therapy for Peyronie's disease. J Urol. 2015;194(3):754–8. https://doi.org/10.1016/j.juro.2015.03.092.
83.• Alom M, Sharma KL, Toussi A, Kohler T, Trost L. Efficacy of combined collagenase Clostridium histolyticum and RestoreX penile traction therapy in men with Peyronie's disease. J Sex Med. 2019;16(6):891–900. https://doi.org/10.1016/j.jsxm.2019.03.007 **This prospective study showed improved outcomes with the use of a traction therapy device in conjunction with CCH therapy. It provides evidence that a combination of therapies may be superior to monotherapy.**
84. Gontero P, Di Marco M, Giubilei G, Bartoletti R, Pappagallo G, Tizzani A, et al. Use of penile extender device in the treatment of penile curvature as a result of Peyronie's disease. Results of a phase II prospective study. J Sex Med. 2009;6(2):558–66. https://doi.org/10.1111/j.1743-6109.2008.01108.x.
85. Levine LA, Newell M, Taylor FL. Penile traction therapy for treatment of Peyronie's disease: a single-center pilot study. J Sex Med. 2008;5(6):1468–73. https://doi.org/10.1111/j.1743-6109.2008.00814.x.
86. Kadioglu A, Akman T, Sanli O, Gurkan L, Cakan M, Celtik M. Surgical treatment of Peyronie's disease: a critical analysis. Eur Urol. 2006;50(2):235–48. https://doi.org/10.1016/j.eururo.2006.04.030.
87. Savoca G, Scieri F, Pietropaolo F, Garaffa G, Belgrano E. Straightening corporoplasty for Peyronie's disease: a review of 218 patients with median follow-up of 89 months. Eur Urol. 2004;46(5):610–4; discussion 3-4. https://doi.org/10.1016/j.eururo.2004.04.027.
88. Bokarica P, Parazajder J, Mazuran B, Gilja I. Surgical treatment of Peyronie's disease based on penile length and degree of curvature. Int J Impot Res. 2005;17(2):170–4. https://doi.org/10.1038/sj.ijir.3901255.
89. Syed AH, Abbasi Z, Hargreave TB. Nesbit procedure for disabling Peyronie's curvature: a median follow-up of 84 months. Urology. 2003;61(5):999–1003.
90. Ralph DJ. al-Akraa M, Pryor JP. The Nesbit operation for Peyronie's disease: 16-year experience. J Urol. 1995;154(4):1362–3.
91. Licht MR, Lewis RW. Modified Nesbit procedure for the treatment of Peyronie's disease: a comparative outcome analysis. J Urol. 1997;158(2):460–3.
92. Yachia D. Modified corporoplasty for the treatment of penile curvature. J Urol. 1990;143(1):80–2. https://doi.org/10.1016/s0022-5347(17)39871-3.
93. Daitch JA, Angermeier KW, Montague DK. Modified corporoplasty for penile curvature: long-term results and patient satisfaction. J Urol. 1999;162(6):2006–9. https://doi.org/10.1016/s0022-5347(05)68088-3.
94. Rehman J, Benet A, Minsky LS, Melman A. Results of surgical treatment for abnormal penile curvature: Peyronie's disease and congenital deviation by modified Nesbit plication (tunical shaving and plication). J Urol. 1997;157(4):1288–91. https://doi.org/10.1016/s0022-5347(01)64953-x.
95. Mufti GR, Aitchison M, Bramwell SP, Paterson PJ, Scott R. Corporeal plication for surgical correction of Peyronie's disease. J Urol. 1990;144(2 Pt 1):281–2; discussion 3. https://doi.org/10.1016/s0022-5347(17)39432-6.
96. Gholami SS, Lue TF. Correction of penile curvature using the 16-dot plication technique: a review of 132 patients. J Urol. 2002;167(5):2066–9.
97. Chahal R, Gogoi NK, Sundaram SK, Weston PM. Corporal plication for penile curvature caused by Peyronie's disease: the patients' perspective. BJU Int. 2001;87(4):352–6.
98. Geertsen UA, Brok KE, Andersen B, Nielsen HV. Peyronie curvature treated by plication of the penile fasciae. Br J Urol. 1996;77(5):733–5.
99. Thiounn N, Missirliu A, Zerbib M, Larrouy M, Dje K, Flam T, et al. Corporeal plication for surgical correction of penile curvature. Experience with 60 patients. Eur Urol. 1998;33(4):401–4.
100. Van Der Horst C, Martinez Portillo FJ, Seif C, Alken P, Juenemann KP. Treatment of penile curvature with Essed-Schroder tunical plication: aspects of quality of life from the patients' perspective. BJU Int. 2004;93(1):105–8.
101. Schultheiss D, Meschi MR, Hagemann J, Truss MC, Stief CG, Jonas U. Congenital and acquired penile deviation treated with the essed plication method. Eur Urol. 2000;38(2):167–71. https://doi.org/10.1159/000020275.
102. Levine LA, Lenting EL. A surgical algorithm for the treatment of Peyronie's disease. J Urol. 1997;158(6):2149–52. https://doi.org/10.1016/s0022-5347(01)68184-9.
103. Wild RM, Devine CJ Jr, Horton CE. Dermal graft repair of Peyronie's disease: survey of 50 patients. J Urol. 1979;121(1):47–50. https://doi.org/10.1016/s0022-5347(17)56657-4.
104. Melman A, Holland TF. Evaluation of the dermal graft inlay technique for the surgical treatment of Peyronie's disease. J Urol. 1978;120(4):421–2. https://doi.org/10.1016/s0022-5347(17)57209-2.

105. O'Donnell PD. Results of surgical management of Peyronie's disease. J Urol. 1992;148(4):1184–7. https://doi.org/10.1016/s0022-5347(17)36854-4.
106. Das S. Peyronie's disease: excision and autografting with tunica vaginalis. J Urol. 1980;124(6):818–9. https://doi.org/10.1016/s0022-5347(17)55682-7.
107. Kargi E, Yesilli C, Hosnuter M, Akduman B, Babuccu O, Mungan A. Relaxation incision and fascia lata grafting in the surgical correction of penile curvature in Peyronie's disease. Plast Reconstr Surg. 2004;113(1):254–9. https://doi.org/10.1097/01.PRS.0000095951.04305.38.
108. Shioshvili TJ, Kakonashvili AP. The surgical treatment of Peyronie's disease: replacement of plaque by free autograft of buccal mucosa. Eur Urol. 2005;48(1):129–33; discussion 34-5. https://doi.org/10.1016/j.eururo.2005.01.018.
109. Teloken C, Grazziotin T, Rhoden E, Da Ros C, Fornari A, Soares FC, et al. Penile straightening with crural graft of the corpus cavernosum. J Urol. 2000;164(1):107–8.
110. Kim ED, McVary KT. Long-term followup of treatment of Peyronie's disease with plaque incision, carbon dioxide laser plaque ablation and placement of a deep dorsal vein patch graft. J Urol. 1995;153(6):1843–6.
111. Hsu YS, Huang WJ, Kuo JY, Chung HJ, Chen KK, Chang LS. Experience of surgical treatment of peyronie's disease with deep dorsal venous patch graft in Taiwanese men. J Chin Med Assoc. 2003;66(8):487–91.
112. Craatz S, Spanel-Borowski K, Begemann JF, Olianas R, Fisch M, Hohenfellner R. The dorsal lamina of the rectus sheath: a suitable grafting material for the penile tunica albuginea in Peyronie's disease? BJU Int. 2006;97(1):134–7. https://doi.org/10.1111/j.1464-410X.2006.05876.x.
113. Gelbard MK, Hayden B. Expanding contractures of the tunica albuginea due to Peyronie's disease with temporalis fascia free grafts. J Urol. 1991;145(4):772–6. https://doi.org/10.1016/s0022-5347(17)38447-1.
114. Kalsi J, Minhas S, Christopher N, Ralph D. The results of plaque incision and venous grafting (Lue procedure) to correct the penile deformity of Peyronie's disease. BJU Int. 2005;95(7):1029–33. https://doi.org/10.1111/j.1464-410X.2005.05459.x.
115. De Stefani S, Savoca G, Ciampalini S, Gattuccio I, Scieri F, Belgrano E. Saphenous vein harvesting by 'stripping' technique and 'W'-shaped patch covering after plaque incision in treatment of Peyronie's disease. Int J Impot Res. 2000;12(6):299–301. https://doi.org/10.1038/sj.ijir.3900633.
116. Montorsi F, Salonia A, Maga T, Bua L, Guazzoni G, Barbieri L, et al. Evidence based assessment of long-term results of plaque incision and vein grafting for Peyronie's disease. J Urol. 2000;163(6):1704–8.
117. Chen R, McCraw C, Lewis R. Plication procedures-excisional and incisional corporoplasty and imbrication for Peyronie's disease. Transl Androl Urol. 2016;5(3):318–33. https://doi.org/10.21037/tau.2016.05.01.
118. Carson CC. Penile prosthesis implantation in the treatment of Peyronie's disease and erectile dysfunction. Int J Impot Res. 2000;12(Suppl 4):S122–6.
119. Levine LA, Dimitriou RJ. A surgical algorithm for penile prosthesis placement in men with erectile failure and Peyronie's disease. Int J Impot Res. 2000;12(3):147–51.
120. Wilson SK, Delk JR 2nd. A new treatment for Peyronie's disease: modeling the penis over an inflatable penile prosthesis. J Urol. 1994;152(4):1121–3. https://doi.org/10.1016/s0022-5347(17)32519-3.
121. Chaudhary M, Sheikh N, Asterling S, Ahmad I, Greene D. Peyronie's disease with erectile dysfunction: penile modeling over inflatable penile prostheses. Urology. 2005;65(4):760–4. https://doi.org/10.1016/j.urology.2004.10.039.
122. Montorsi F, Guazzoni G, Barbieri L, Maga T, Rigatti P, Graziottin A, et al. AMS 700 CX inflatable penile implants for Peyronie's disease: functional results, morbidity and patient-partner satisfaction. Int J Impot Res. 1996;8(2):81–5 discussion 5-6.
123. Austoni E, Colombo F, Romano AL, Guarneri A, Kartalas Goumas I, Cazzaniga A. Soft prosthesis implant and relaxing albugineal incision with saphenous grafting for surgical therapy of Peyronie's disease: a 5-year experience and long-term follow-up on 145 operated patients. Eur Urol. 2005;47(2):223–9; discussion 9. https://doi.org/10.1016/j.eururo.2004.10.004.
124. Montague DK, Angermeier KW, Lakin MM, Ingleright BJ. AMS 3-piece inflatable penile prosthesis implantation in men with Peyronie's disease: comparison of CX and Ultrex cylinders. J Urol. 1996;156(5):1633–5.
125. Usta MF, Bivalacqua TJ, Sanabria J, Koksal IT, Moparty K, Hellstrom WJ. Patient and partner satisfaction and long-term results after surgical treatment for Peyronie's disease. Urology. 2003;62(1):105–9.