EDITORIAL

Unveiling treatment horizons and contemporary perspectives in Peyronie's disease – take home messages from Laurance A. Levine special issue

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This special issue of IJIR: Your Sexual Medicine Journal focuses on Peyronie's disease (PD). A more common than previously thought and very troubling disorder for the effected man. A variety of subjects are addressed in this issue, and as expected, most articles focus on new and old avenues of treatment. The variety of options offered since the time of de la Peyronie is staggering, and yet we still do not have a reliable, safe, effective, non-surgical treatment. This likely reflects our lack of understanding of the pathophysiology of this disorder of wound healing. Let's briefly review those articles.

The newest addition to topical therapy is H100 gel. This is a combination of nicardipine and super oxide dismutase in an Emu oil delivery solution to enhance tissue penetration. Previous work on this agent did show, in a small, controlled, crossover study a positive signal of benefit with respect to measured reduction of curvature and length [1].The paper in this issue is sponsored by the manufacturer, and attempts to answer the question as to whether the active ingredient is found in the target tissue after topical application [2]. In this small study, all 3 men who had daily application of the H100 gel did have measured levels of nicardipine in the tunica albuginea. As to the concentration needed to cause tissue change, this is not known. But, as a noninvasive, nontoxic treatment, it may be appealing to many men with mild-moderate deformity.

The next article is an extensive bibliographic analysis of the PD literature between 1946 and 2016, reporting on the 100 most cited papers on PD [3]. This study demonstrated that The University of California, Los Angeles, was the institution with the largest number of articles ($n = 11$). The author with the most articles was Levine LA ($n = 9$) whereas Gelbard MK's articles had the highest citation frequency ($n = 1158$).

A useful contemporary review on how patients are presenting to a PD Center of Excellence provides insights to the patients that we currently see in our offices. From this paper we learn that these men often present late for evaluation, only 29% remembered a traumatic event preceding their PD symptoms, a much larger than expected number of patients had indentation or narrowing deformity, often referred to as volume loss with 76% having this deformity and 30% had calcification noted on ultrasound as early as 6 weeks after onset of symptoms. Even in this center, which is known to favor surgical treatment, only 35% did undergo surgery. Multi-variant analysis demonstrated that curvature greater than 60°, hour-glass deformity and prior failure of treatment with collagenase Clostridium Histolyticum (CCH) were found to predict surgery [4].

I am not a big fan of large-scale claims database analyses. But, the article using this format to determine the rate of PD and erectile dysfunction (ED) after penile fracture was interesting, indicating a higher rate of both problems in men over 45 years old who were treated conservatively vs men under 45 years [5].

There are two interesting articles that suggest potential benefits to taking an oral phosphodiesterase type 5 inhibitor (PDE5i) during the acute phase of PD. Daily use was reported to potentially reduce penile curvature progression rate in one article, whereas the other reported a shortening of pain duration. There are two commentaries which note potential serious flaws in study design in both articles which may weaken the argument of their therapeutic benefit, but these authors make the point that these studies hopefully will encourage more carefully performed analyses in the future [6–9].

Here again we find a paper beating the shockwave therapy for PD drum. This 10-year retrospective analysis showed once more, no improvement in deformity, but maybe a reduction in pain [10]. My hope is that the practicing urologist or healthcare provider seeing these patients will stop offering shockwave treatment of any sort, as there has never been a demonstrated improvement of deformity as a result of using any type of shockwaves.

A new combination therapy approach is offered with percutaneous needle tunneling, presumably to create channels into the hypo-vascular and hypo-cellular scar tissue, to more effectively deliver platelet-rich-plasma (PRP) [11]. This paper comes from Montpellier France, the home of de la Peyronie. A thoughtful commentary follows [12]. The authors state that this treatment is both safe and feasible. The real answer as to the efficacy will come with larger scale, multi-center studies with at least one year of follow-up.

I recently conducted my own literature review of nonsurgical treatment since the early 2000's, including a variety of injection therapies (verapamil, CCH, interferon, hyaluronic acid, PRP), traction and vacuum, which showed a mean curve reduction ranging from 5 to 25°. The point being that, so far it appears that non-surgical treatment would likely be best for men with mild-moderate curve, if the goal is to make the man functionally straight with these treatments, which we previously defined as less than 20° [13].

A new surgical approach to penile straightening as well as possible length and girth recovery is reported in this issue [14]. The surgery is a modification of the tunic expansion procedure performed through a peno-scrotal incision to presumably reduce the risk of distal shaft skin and glans ischemia. This innovative approach was used in 32 patients with no reported tissue loss or infection. The authors consider the surgery "easy to perform". A supportive commentary follows [15]. Our own institution's experience with a single-incision subcoronal approach for correction of deformity including incision and grafting and

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placement of a 3-piece prosthesis was recently published showing a low rate of any skin or glans tissue loss at 1.5% in 66 consecutive patients [16].

A survey on the exposure to the use of Xiaflex (CCH) for PD among 47 United States urology training programs found the unexpectedly low level of 66%, while 98% of these programs stated that they provided surgical training for PD. This may reflect lack of a faculty champion for CCH, but may also be associated with local resistance to CCH use due to cost and reported outcomes with Xiaflex [17].

There is also an interesting report using another research registry, TriNetX, examining treatment pathways which shows most men (72%) presenting with PD received no treatment, while 24.5% of those who progressed from medical therapy ultimately underwent a surgical procedure [18]. Clearly, most patients as found in the previous report by Roadman et al. [4], do not need or want surgery, but those with severe deformity should not be directed into expensive and invasive treatment simply because it is approved by the FDA or because the treating physician has limited experience with surgery or is not confident with their results.

The final paper in this issue asks the question- "Can we try to avoid surgery first?" which translates to whether all patients should be given an opportunity to undergo multiple courses of CCH treatment before surgery is considered [19]. It is my opinion that in the acute phase, surgery is not indicated unless the patient has already demonstrated drug-refractory erectile dysfunction and will need a penile prosthesis. Clearly nonsurgical therapy should be offered to any man in the acute phase, or in the stable phase, should they not be interested in surgery. Our own experience with patients who failed CCH and ultimately underwent surgery indicated that the majority had curvature greater than 60°, had severe indentation deformity causing hinge-effect and/or had extensive calcification [20]. My concern with this last paper is that the suggestion is that if 8 CCH injections does not adequately correct the deformity, consider using 16, 24 or more of these very costly treatments. It is my feeling that the clear point here is that patient preference needs to be recognized. Some men insist on optimum correction which will almost always be accomplished with surgery as an outpatient procedure with recognized and limited side effects when the patient is properly selected, and the surgery is performed by an experienced surgeon. On the other hand, many patients would never consider surgery and should be offered nonsurgical treatment, and if they are making progress after an initial course of CCH then a second course may make sense. But giving repeated courses of CCH appears to have diminishing returns for many patients on top of a big investment in time and money.

To sum up, this special edition on PD has shed some new light on the disorder's complexity and provided some useful information on its causes, manifestations, and treatment options. Providing the best care possible to those with this ailment requires a holistic approach that integrates medical, surgical, and psychological perspectives. This is evident as we navigate the condition's complex environment. As caregivers we open the door for future advancements in the field of PD by supporting ongoing research and promoting communication between researchers, patients, and healthcare professionals. My hope is that this will ultimately improve the quality of life for individuals who are impacted by this difficult condition.

Laurance A. Levine[1]✉
[1]*International Journal of Impotence Research https://www.nature.com/ijir/.* ✉*email: drlevine@hotmail.com*

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