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## Nonsurgical Management of Peyronie's Disease—Are We Making Any Progress?

**M**anagement of Peyronie's disease remains one of the most vexing issues in sexual medicine. Described in 1743 by Francois Gigo de LaPeyronie, First Surgeon to King Louis XV, the etiology of this condition continues to be a topic of debate.<sup>1</sup> Due in part, perhaps, to our incomplete understanding of the pathogenesis of Peyronie's disease, the nonsurgical treatment of this entity has progressed surprisingly little since Peyronie described 3 cases being cured by the healing waters of the thermal springs at Baréges.<sup>2</sup>

The prevalence of Peyronie's disease has been estimated to be 3.2% among men 30 to 80 years old.<sup>3</sup> With the introduction of phosphodiesterase type 5 inhibitors and the attendant efforts to encourage men with erectile dysfunction to openly discuss this problem with medical providers, sexual dysfunction has shifted from a taboo subject to a common topic of physician-patient discussions. One of the benefits of this climate of improved communication is that men with other types of sexual dysfunction such as premature ejaculation and decreased libido may also be more likely to seek help. In a similar vein, men with Peyronie's disease will likely be more at ease discussing the seemingly mysterious changes in penile morphology and function that are part of this condition. For this reason, as well as the general aging of our population, the management of Peyronie's disease will likely comprise an increasing part of urological practice in the years to come.

The surgical management of Peyronie's disease has been relatively effective in correcting penile curvature. Plication procedures have proven to be safe and effective but are associated with penile shortening.<sup>4</sup> The technique of plaque excision has advanced over the years, incorporating the interposition of a variety of substances to fill the resulting corporeal defect. Penile prosthesis implantation has assumed a primary role in the treatment of patients with Peyronie's disease who experience severe, refractory erectile dysfunction.<sup>5</sup>

Unfortunately the nonsurgical management of Peyronie's disease has not kept pace with the surgical treatment of this condition. This discrepancy has led to tremendous frustration among patients who do not wish to proceed with surgical correction but for whom the pain, disfigurement and sexual dysfunction are a constant source of anxiety and distress. Multiple nonsurgical remedies including a variety of oral, topical and injectable agents, as well as more novel approaches such as extracorporeal shock wave lithotripsy, have been deployed to alter the clinical course of Peyronie's disease.<sup>5-7</sup> However, as is often the case when multiple unrelated treatments exist for a single condition, the evidence demonstrating the effectiveness of these remedies in the management of Peyronie's disease has been sparse at best.

Substantial attention has recently been directed toward the injection of pharmacological agents directly into Peyronie's lesions in an effort to induce plaque remodeling and diminish fibrosis. Plaque injection is less convenient than oral or topical agents, requiring repeated trips to a physician's office. Moreover, injection is typically associated with moderate discomfort and penile ecchymosis. However, if demonstrated to be effective, such therapy would almost certainly be preferable to surgery for many patients. One of the larger recent studies involved intralesional injection of verapamil in 156 men with Peyronie's disease, 140 of whom completed treatment.<sup>8</sup> Although the study did not include a placebo arm, the results suggested that such therapy was associated with substantial improvement in pain, penile curvature and sexual function.

In this issue of *The Journal* Hellstrom et al (page 394) present the results of a multicenter, placebo controlled, single blind trial of intralesional injection of interferon alpha-2b for the treatment of Peyronie's disease. This study serves as followup to previous pilot studies involving intralesional injection of interferon in the treatment of this condition.<sup>9,10</sup> Notably, the design of this study included a placebo arm (plaque injection with saline), which has been lacking in many protocols investigating nonsurgical methods for treating Peyronie's disease. A total of 103 subjects completed the study (53 in the saline injection group and 50 in the interferon injection group). The results of this study were encouraging in that subjects receiving interferon injections experienced improvement in penile curvature, decreased plaque size and density, and reduced pain compared to those who received intralesional saline injection. Subjects receiving interferon injections were also demonstrated to have improved penile blood flow following therapy as assessed by penile duplex Doppler ultrasonography. Interestingly there was no significant difference in improvement in sexual function as assessed by International Index of Erectile Function evaluation when comparing subjects treated with interferon vs those treated with placebo. While interferon injections were associated with systemic side effects such as sinusitis, fever, chills and arthralgia, such side effects were of limited duration (none lasting longer than 36 hours) and were effectively managed with over-the-counter nonsteroidal anti-inflammatory agents.

Interestingly, in this study intralesional injection of 10 ml of saline was associated with statistically significant improvements in penile curvature, plaque size and plaque density. The authors suggest that this phenomenon may be due to hydrostatic pressure exerted by the injected saline leading to induction of local factors that contribute to plaque remodeling. Although the impact of intralesional interferon injection on all 3 of the parameters exceeded that of intralesional saline injection, it is worth noting that saline injection alone

resulted in significant improvement in the absence of a pharmacologically active agent. It is difficult to determine the extent of the placebo effect in this setting since the placebo itself appears to have had a substantial therapeutic impact. Although the authors believe that the results following saline injection were better than would have been expected in the absence of intervention, the addition of a control arm in which subjects received no treatment would likely have been highly informative.

The design of this study should serve to raise the bar for future investigative efforts regarding the effectiveness of nonsurgical therapies for Peyronie's disease. Large scale, randomized, placebo controlled trials using objective end points will almost certainly be necessary if further meaningful progress is to be made in the management of this pernicious affliction. Had Francois de LaPeyronie known how things would progress when he put ink to paper 263 years ago, he might well have chosen another topic . . .

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