

## SEXUAL MEDICINE REVIEWS

## Review of Management Options for Patients With Atypical Peyronie's Disease

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## ABSTRACT

**Introduction:** Peyronie's disease (PD) is a wound-healing disorder of the tunica albuginea often associated with penile deformity. Less commonly, patients with PD might display atypical presentations such as ventral curvature, hourglass deformity, significantly shortened penis, and/or multiplanar curvature.

**Aim:** To review the available literature on the prevalence of and management options for atypical PD.

**Methods:** A literature review was performed through PubMed from 1982 through 2016 regarding atypical PD. Keywords used for the search were *Peyronie's disease*, *atypical Peyronie's disease*, *ventral Peyronie's disease*, *ventral plaque*, *hourglass deformity*, *penile indentation*, *penile notching*, *short penis*, *shortened penis*, *shrunken penis*, *biplanar curvature*, and *multiplanar curvature*.

**Main Outcome Measures:** To assess the various surgical and non-surgical techniques used for the management of atypical PD.

**Results:** Collagenase *Clostridium histolyticum* is contraindicated for patients with ventral plaques and/or hourglass deformities. Patients with maintained erectile function and ventral PD plaques are best treated with intralesional injections of interferon alpha-2b or tunica plication. Patients with maintained erectile function with PD associated with hourglass deformity and/or multiplanar curvature are best treated with plaque incision or partial excision and grafting. Patients with a shortened penis could attempt conservative measures such as penile traction therapy and medical management. When erectile function is compromised, insertion of an inflatable penile prosthesis with or without ancillary straightening procedures should be recommended. Lengthening procedures can be attempted in very special circumstances by expert surgeons.

**Conclusion:** There is a paucity of data regarding atypical PD. Ventral plaques can be treated with intralesional injections or surgery, hourglass deformity and multiplanar curvatures are best managed surgically, and a shortened penis should be treated with non-invasive approaches. When concomitant erectile dysfunction is present, insertion of an inflatable penile prosthesis is recommended. Caution should be advised before undergoing ancillary penile lengthening maneuvers owing to the potential for serious complications.

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**Key Words:** Peyronie's Disease; Ventral Plaque; Hourglass Deformity; Shortened Penis; Atypical Peyronie's Disease

## INTRODUCTION

Peyronie's disease (PD), first described by French surgeon François Gigot de LaPeyronie, is a wound-healing disorder of the tunica albuginea of the penis.<sup>1,2</sup> Historically believed to be a rare entity, new epidemiologic data have emerged suggesting a

significantly higher prevalence with close to 1 in 10 men being diagnosed with this condition.<sup>3–6</sup> Accordingly, more research has been conducted in recent times with the aim of better understanding the pathophysiology, genetics, and natural progression of PD and the management options for patients with this condition.

The acute phase of the disease presents with penile pain on erection and progressive penile curvature. The pain is usually self-limited and, in most cases, resolves within a year. The chronic phase marks the end of the inflammatory insult and stabilization of the penile curvature or abnormality and usually occurs within 12 to 18 months after onset.<sup>1</sup> On the microscopic level, PD presents as a disorganized, excessive deposition of

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collagen, resulting in the formation of a plaque within the penile tunica albuginea. This in turn can lead to penile curvature, deformity, discomfort, pain, and/or erectile dysfunction (ED).<sup>1</sup> Ultimately, many men with PD experience emotional distress, depressive symptoms, and relationship difficulties.<sup>7,8</sup>

Most men will present to the clinic with a palpable plaque and a uniplanar dorsolateral curvature.<sup>1</sup> In rare circumstances, they might present with various “atypical” presentations, often precluding them from receiving routinely recommended intralesional and surgical treatment options. These include ventral curvature, hourglass deformity, severely shortened penis, and bi- or multiplanar curvatures. We sought to review the available literature regarding these atypical PD presentations and highlight the optimal therapeutic options for management of each of these conditions. For this purpose, a literature review was performed through PubMed from 1982 through 2016 regarding atypical PD. Keywords used for the search were *Peyronie’s disease*, *atypical Peyronie’s disease*, *ventral Peyronie’s disease*, *ventral plaque*, *hourglass deformity*, *penile indentation*, *penile notching*, *short penis*, *shortened penis*, *shrunk penis*, *biplanar curvature*, and *multiplanar curvature*.

## VENTRAL PLAQUE

PD plaques most commonly manifest on the dorsal or dorsolateral aspects of the penile shaft.<sup>9</sup> Less frequently, in approximately 9% of cases, these plaques can occur on the ventral aspect of the penis, ultimately leading to a ventral or downward deviation of the penis at erection. Until recently, owing to its low prevalence, there had been a paucity of reports and publications that discussed the frequency of and management options for ventral PD. [Table 1](#) presents the published and non-published studies evaluating treatment options for patients with atypical PD.

For patients with PD and poor erectile function that is non-responsive to medical therapy, the consensus is to proceed with insertion of an inflatable penile prosthesis (IPP) with or without ancillary straightening procedures such as manual modeling, penile plication, tunica incision, and grafting.<sup>17–19</sup> The main benefit of this approach is the ability to address the penile deformity and the ED with one intervention. The same principles hold true for patients with ventral PD and significant concomitant ED.

The real dilemma is how to approach patients with a ventral curvature and preserved erectile function. If a patient presents in the active phase of the disease, manifested by symptoms such as worsening plaque or persistent pain on erection, then it is not unreasonable to consider less invasive interventions such as oral medications, shock wave therapy, and/or penile stretching therapy. Although these modalities might, to a certain degree, help decelerate the disease process, relieve pain, and avoid further loss of penile length, they are unlikely to straighten the curvature.<sup>1,2</sup>

Historically, surgery has been the gold standard management option for the treatment of PD in its stable phase.<sup>1,2</sup> In more

recent years, owing to the potential complications associated with surgery, an impetus has been placed on finding less invasive interventions, such as intralesional injection (ILI) therapy.

Owing to their anti-inflammatory properties, corticosteroids were the first intralesional drugs to be investigated for the management of PD.<sup>20</sup> Although initial studies did demonstrate some minimal benefit, further reports did not replicate these results, and, as such, they have fallen out of favor and are no longer used.<sup>20,21</sup> Intralesional verapamil, a calcium channel blocker with fibroblast-regulating anti-inflammatory effects, was first investigated for the management of PD in 1994.<sup>22</sup> Since then, multiple reports have been published, with mixed results.<sup>23,24</sup> Berookhim et al<sup>10</sup> recently investigated ILI of verapamil and demonstrated safety and comparable efficacy for ventral (40% curvature improvement with treatment) and dorsal (25% improvement) injections. Interferon alpha-2b (IFN) is believed to decrease the rate of fibroblast proliferation, decrease the production of extracellular collagen, and increase the production of collagenase.<sup>25</sup> Multiple studies have demonstrated that ILI of IFN imparts significant benefits in penile curvature, plaque size and density, and pain resolution compared with placebo.<sup>26,27</sup> In a further analysis by the same group and a total of 131 patients (111 with dorsal curvature and 21 with ventral curvature), no significant difference was noted between the two groups regarding response rate (54% vs 52%,  $P = .92$ ) or absolute change in curvature (mean =  $8.7 \pm 12.6^\circ$  vs  $9.3 \pm 17.7^\circ$ ,  $P = .84$ ).<sup>11</sup> Of note, no notable serious complications were observed with ventral injections.

Collagen *Clostridium histolyticum* (CCH) is a biological agent that enzymatically degrades interstitial collagen present in PD plaques.<sup>28</sup> In two landmark studies, Investigation for Maximal Peyronie’s Reduction Efficacy and Safety Studies (IMPRESS) 1 and 2, ILI of CCH demonstrated a mean 34% improvement in penile curvature compared with a mean 18.2% improvement in placebo-treated men ( $P < .0001$ ), and the mean change in PD symptom bother score was significantly improved in treated men vs men on placebo ( $-2.8$  vs  $-1.8$ ,  $P = .0037$ ).<sup>29</sup> Of note, three serious treatment-related corporal ruptures requiring surgical intervention occurred in patients who were believed to have had strenuous sexual intercourse within 2 weeks of injection.

Based on the positive results of the IMPRESS trials, ILI of CCH became the first and only drug approved by the Food and Drug Administration for the management of PD.

Unfortunately, one of the trials’ exclusion criteria was ventral location of plaque owing to the concern of urethral injury. As such, ILI of CCH is currently not approved by the Food and Drug Administration for ventral PD. In a recently presented scientific abstract, Milam<sup>12</sup> described ILI of CCH to two patients with ventral PD. The two men experienced clinically significant improvement in curvature with treatment ( $45^\circ$  to  $5^\circ$  and  $30^\circ$  to  $5$ – $10^\circ$ , respectively, at the time of the fourth cycle), with neither patient experiencing urethral side effects other than local discomfort and minor bruising. Further evidence of the

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