

# Peyronie's disease:

## knowing when to treat the condition

### Key points

- Peyronie's disease is characterised by a curvature of the penile shaft, particularly during erections, that is usually associated with a palpable area of fibrosis in the tunica albuginea.
- The prevalence of Peyronie's disease is probably underestimated because of the embarrassment most men feel about having this condition.
- Most men present with penile pain, penile angulation, a plaque that is usually palpable at the site of and on the acute side of the angulation, an indentation in the shaft and/or decreased erectile function.
- Most men require only reassurance and a watchful waiting approach.
- Peyronie's disease should be debilitating, prohibiting satisfactory intercourse, if surgery is to be performed.

**BENJAMIN DAVIDSON** MB BS(Hons), BSc(Hons), PhD(Biochem)  
**PETER SUTHERLAND** MB BS, FRACS

**Peyronie's disease can be a debilitating condition affecting a man's sexual function. A six-month duration of stable, not worsening, symptoms is necessary before surgical treatment can be considered. Otherwise, watchful waiting and patient reassurance are all that are needed.**

**F**rançois Gigot de la Peyronie is widely credited as being the first person to describe penile curvature in 1743, a condition now known as Peyronie's disease.<sup>1</sup> Peyronie's disease is characterised by a curvature of the penile shaft, particularly during erections, that is usually associated with a palpable area of fibrosis in the tunica albuginea. It is often preceded by painful erections and is frequently associated with erectile dysfunction, either as a result of buckling of the penile shaft with intromission or because of a lack of rigidity distal to the area of associated fibrosis. This lack of rigidity seems to be the result of a compromise in the distal

penile blood supply.

The curvature is usually obvious when the penis is erect but is occasionally also noticeable when the penis is flaccid. The fibrotic area, known as a plaque, can vary in firmness and sometimes becomes calcified. Although the name Peyronie's disease implies that this condition is a disease, it is not associated with an infecting organism and cannot be transmitted from one person to another.

Over the years, various medical and surgical therapies have been used to treat men with Peyronie's disease. The number and variety of these attempts at treatment stand as a testament to their relative lack of effectiveness.

Dr Davidson is Senior Registrar in the Intensive and Critical Care Unit at Flinders Medical Centre, Adelaide. Dr Sutherland is Head of the Urology Department at The Royal Adelaide Hospital and is in private practice in Adelaide, SA.

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## PREVALENCE

The prevalence of Peyronie's disease is reported to be from 0.39 to 3%.<sup>2-3</sup> However, this is probably an underestimation because of the embarrassment most men feel about having this condition. The true prevalence may be approaching 10%.<sup>4</sup> Under-reporting of Peyronie's disease may also be the result of a lack of men seeking assistance when their symptoms are mild or nondebilitating. Although this condition usually affects men aged 40 to 70 years, it can also occur in younger individuals. A significant proportion of men with Peyronie's disease also have hypertension and diabetes.<sup>5</sup>

## AETIOLOGY

Despite the medical community having recognised Peyronie's disease for about 250 years, the aetiology of the condition remains unclear. Current thinking is that Peyronie's disease is a disorder of inappropriate wound healing and as such may be considered similar to the formation of hypertrophic (keloid) scars.

The development of Peyronie's disease probably results from vascular trauma or injury to the penis (Figure 1). The injury may be trivial or involve only microscopic vessels and tissues as can happen unnoticed during intercourse. This triggers the release of cytokines that activate fibroblast proliferation and produce collagen, the main matrix component of a Peyronie's plaque, within the tunica albuginea (Figures 2a and b).

Other risk factors for Peyronie's disease include a genetic predisposition in association with a family history of Dupuytren's contracture, and systemic vascular diseases such as diabetes mellitus, hypertension and hyperlipidaemia.<sup>6</sup> Smoking and alcohol consumption also increase risk.

## PATHOPHYSIOLOGY

In Peyronie's disease, the initial inflammatory response is characterised by chronic lymphocytic and plasmacytic infiltration of the tunica albuginea as a result of minor penile trauma. Such trauma can result in a dorsal and ventral delamination injury to the tunica albuginea, causing inflammation, induration and fibrin

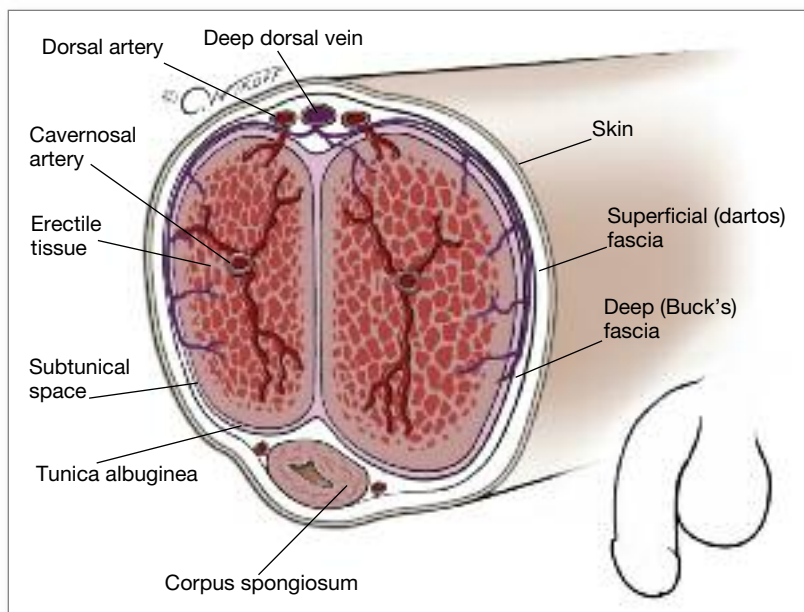


Figure 1. Anatomy of the penis demonstrating the fascial layers and the vascular supply.

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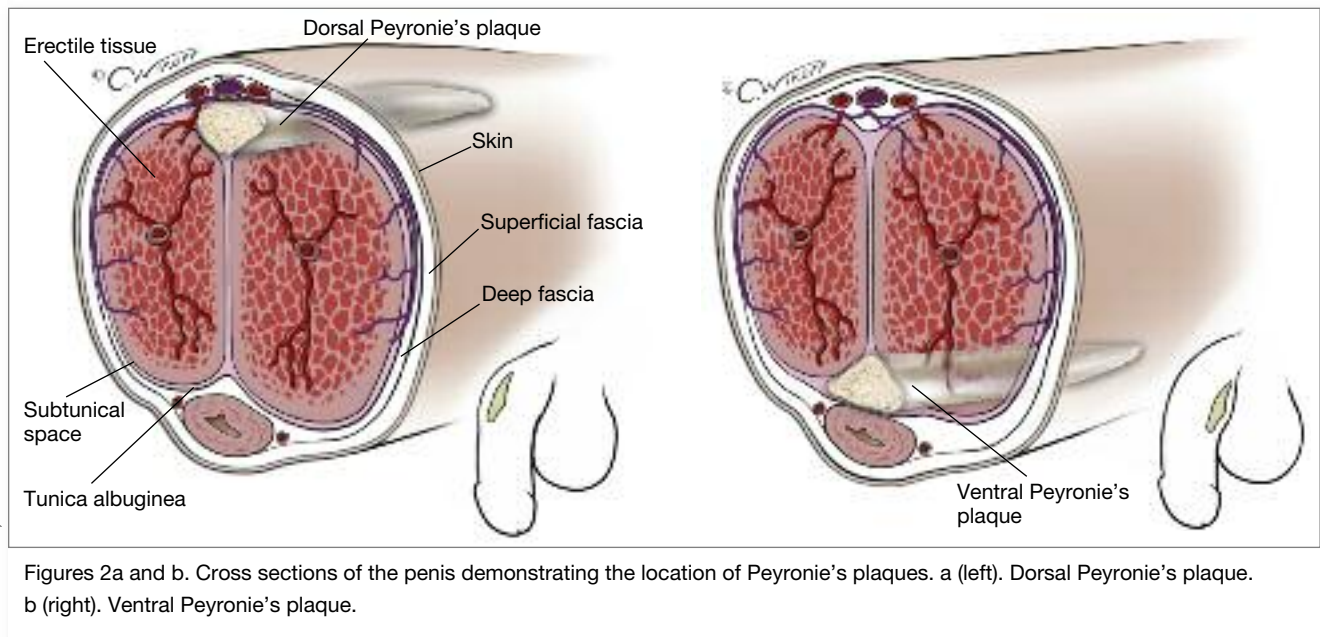
deposition between the tunical layers. If scar tissue formation and extracellular matrix deposition exceed collagen and matrix degradation then increased collagen is deposited in the tunica albuginea, resulting in fibrosis and plaque formation.<sup>7</sup>

## PRESENTATION

The natural history of Peyronie's disease is variable and most men present with any combination of the following:

- penile pain, which is more pronounced during erections
- penile angulation, which may be apparent only with an erection or may be noted in a flaccid penis
- a plaque that is usually palpable at the site of and on the acute side of the angulation
- an indentation in the shaft, typically at the site of the plaque (causing an hour-glass deformity in the shaft)
- decreased erectile function, either from loss of rigidity or from penile buckling caused by the angulation.

For practical purposes, Peyronie's disease can be divided into an acute and a chronic phase. The acute phase of the condition



Figures 2a and b. Cross sections of the penis demonstrating the location of Peyronie's plaques. a (left). Dorsal Peyronie's plaque. b (right). Ventral Peyronie's plaque.

usually lasts for six to 12 months and is characterised by a changing inflammatory pattern that may include penile pain, some curvature and a palpable penile nodule. The chronic phase is characterised by a stable plaque, often with calcification, and penile angulation. Loss of erectile ability is associated more often with the chronic phase.<sup>8</sup>

Earlier studies described Peyronie's disease as being a self-limited condition, with spontaneous resolution in most cases. However, this does not appear to be accurate, with studies indicating Peyronie's disease completely resolves without treatment in only 10 to 20% of men. As spontaneous resolution is unlikely in most men, most investigators recommend intervention if and when the condition impacts significantly upon sexual function. The earlier that medical intervention is initiated, the more likely it is to be successful.<sup>8</sup>

## TREATMENT

By far the most important aspect of treating men with Peyronie's disease is reassurance. Most patients present with a palpable lump and fear that they have

cancer. Initial reassurance is vital and the majority of men will only require support and reassurance. The goal of therapy is to maintain the sexual activity of men with Peyronie's disease and providing education about the disease and its course is often all that is required.

There is no strong evidence showing that any treatment other than surgery is effective. Experts usually recommend surgery only in long-term cases in which the disease is stabilised and the deformity prevents sexual intercourse.

## Medical therapy

The optimum medical therapy for men with Peyronie's disease has not yet been identified. If the pain and/or curvature are minimal and do not preclude normal sexual function, refraining from medical treatment and observing the patient are reasonable. Observation can continue as long as the symptoms remain stable.

Unfortunately, oral pharmacotherapy has shown little success in improving penile pain, curvature and plaque size in patients with Peyronie's disease. There have been a limited number of long-term placebo-controlled studies with oral

agents and, for the most part, studies have failed to show a consistent beneficial effect.

Good evidence is emerging for newer novel intralesional therapies using various agents, such as collagenase, verapamil and interferon. The intralesional approach allows for direct delivery of a particular agent at a concentration that might otherwise be toxic systemically. However, these therapies are still considered experimental and are only administered under the care of a urologist. All of the current and prior therapies along with their presumed modes of action and effectiveness are summarised in Table 1.<sup>9-16</sup>

With patients presenting in the acute phase of the condition, most physicians would prescribe three to six months of oral vitamin E (at a once daily dose of 400 IU) because it has few side effects and may shorten the duration of the acute phase. It is worth noting that although phosphodiesterase-5 (PDE-5) inhibitors have no effect on the progression or treatment of men with Peyronie's disease, they are very useful in treating men with erectile dysfunction, one of the major symptoms associated with Peyronie's disease.

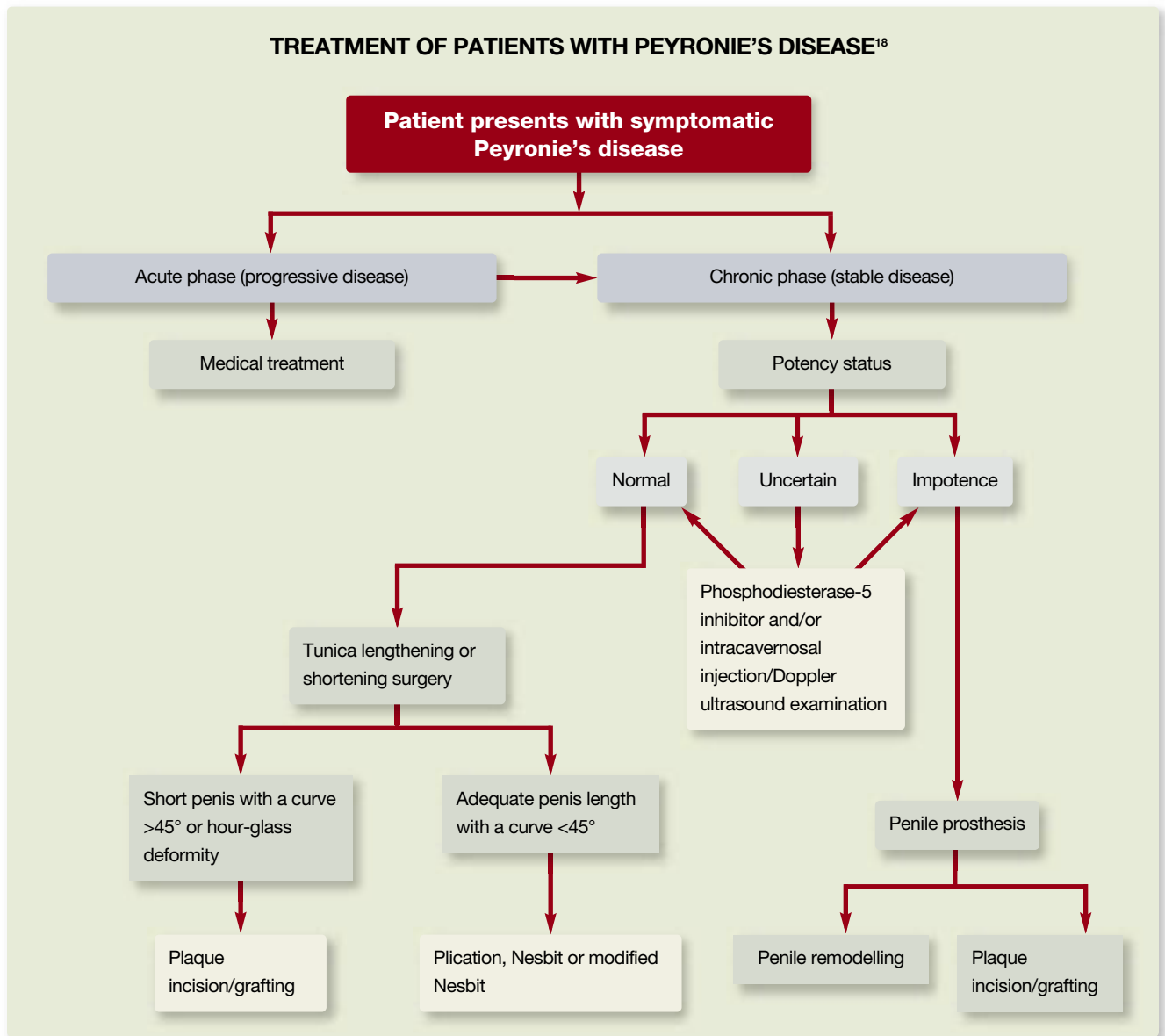
**TABLE. SUMMARY OF THE MEDICAL THERAPIES USED TO TREAT MEN WITH PEYRONIE'S DISEASE<sup>9-16</sup>**

Treatment	Mechanism of action	Comments
<b>Oral and topical therapy</b>		
Vitamin E	Antioxidant that theoretically reverses pathological changes in the tunica albuginea	Efficacy not proven. Has limited side effects and is low cost
Colchicine	Inhibits fibrosis and collagen deposition	Single randomised controlled trial failed to show benefit. Causes gastrointestinal disturbances
Potassium aminobenzoate	Vitamin B complex that may decrease fibrogenesis	Significant reduction in plaque size but not curvature. Expensive and causes gastrointestinal side effects
Tamoxifen	May reduce fibrogenesis	Efficacy not proven
Carnitine	Believed to inhibit acetyl coenzyme A	Efficacy not proven
L-Arginine	Amino acid substrate in the formation of nitric oxide, possibly lacking in Peyronie's disease tissue	Efficacy not proven
Pentoxifylline	Nonspecific phosphodiesterase inhibitor, may reduce collagen levels in Peyronie's disease plaques	Efficacy not proven
Verapamil	Increases collagenase and decreases collagen and fibronectin, inhibits fibroblasts	Efficacy not proven
<b>Intralesional therapy</b>		
Corticosteroids	Anti-inflammatory, reduces collagen synthesis	Unpredictable effects. May cause atrophy. Use not recommended
Collagenase	Breakdown of collagen	Statistically significant improvement in curvature in men with mild to moderate disease
Verapamil	Same as topical verapamil (see above)	Improvements in plaque volume, pain and curvature
Interferon	Decreases fibroblast proliferation. Reduces collagen, increases collagenase	Recent encouraging results with reports of improvements in curvature and pain
Penile ESWT	Induces inflammatory response, improved vascularity, contralateral scarring	Efficacy not proven
EA verapamil +/- dexamethasone	Electric current may have some beneficial effect on wound healing	Improvements in plaque size and curvature
<b>Combination therapy</b>		
Vitamin E with colchicine	Synergistic effect possible	Improvements in curvature and plaque size have been noted
ESWT with intralesional verapamil injection	Synergistic effect possible	Significant improvement in plaque size compared with placebo
Intralesional verapamil injection with carnitine	Synergistic effect possible	Significant subjective improvements in curvature, plaque size and erectile function
Penile traction devices	Stretching of contracted tissue, possible formation of new connective tissue.	Improvement in curvature, increase in length and improvement in hinge effect

ABBREVIATIONS: EA = electrical administration; ESWT = extracorporeal shock wave therapy.



TREATMENT OF PATIENTS WITH PEYRONIE'S DISEASE<sup>18</sup>



**Surgical therapy**

*Indications for surgery*

Before surgical intervention is contemplated, certain criteria should be met. A sufficient duration since the inception of symptoms should elapse to ensure that the condition is stable and to be certain that spontaneous resolution will not occur. If plaque excision is performed before the process of fibrosis is complete, the procedure will fail because further plaque and subsequent curvature will develop.

A sufficient duration is determined by the severity and debilitating effects of the symptoms. It should be in the range of one to two years. During this time, non-surgical treatments can be applied.

If the plaque and/or penile angulation have remained unchanged for six months, then it can be assumed that the condition is stable, and surgical intervention can be contemplated. The associated finding of erectile dysfunction that is not responsive to medication therapy is also an

indication to use surgical approaches that treat both the curvature and the erectile dysfunction.

Peyronie's disease should be debilitating, prohibiting satisfactory intercourse, if surgery is to be performed. Operating to correct small curvatures simply for cosmetic reasons is unreasonable. Usually some degree of curvature remains after surgery, either from residual disease or resultant scar tissue. These patients are usually not satisfied with the results.

It is vital that patients are counselled regarding surgical outcomes. Approximately 1 cm of length is lost for every 10° of curvature. Grafting procedures do not have this complication; however, these procedures have the complication of potentially increasing erectile dysfunction.

### Surgical categories

Three surgical categories exist for men with Peyronie's disease:

- tunica lengthening procedures
- tunica shortening procedures
- implantation of penile prosthesis.<sup>17-19</sup>

Surgical choices for patients require individualisation. Penile prosthesis implantation is reserved for men with refractory erectile dysfunction. Men with satisfactory erectile function with or without medications are candidates for tunica lengthening or shortening procedures. Tunica shortening procedures include Nesbit, or modified Nesbit, and plication techniques. Tunica lengthening procedures include plaque incision or excision and grafting.

Assessing a patient's erectile status is a key step in selecting the appropriate surgical option. Potency may be determined by history, a test of a PDE-5 inhibitor or intracavernosal injection/Doppler ultrasound (ICI/DUS) examination. Patient reports of a rigid erection are sufficient to proceed with a tunica lengthening or shortening procedure. However, many men with Peyronie's disease avoid sexual contact because of penile deformity, and are uncertain of their potency. In these individuals, a trial of PDE-5 inhibitors and subsequent follow-up reports on the adequacy of erections can be valuable in surgical decision-making.

When erectile status is unclear or erectile dysfunction is likely, ICI/DUS is helpful in revealing abnormalities in penile haemodynamics, plaque location and size, and degree of curvature. Large calcified plaques are poor prognostic indicators for spontaneous resolution of

Peyronie's disease or response to medications. Tunica lengthening procedures are appropriate in men with adequate erectile function, shorter penis, curvature of more than 45° or hour-glass deformities. Meanwhile, tunica shortening procedures are indicated in men with good erectile function, adequate penile length or curvature of less than 45° (see the flow-chart on page 50).<sup>18</sup>

### CONCLUSION

Peyronie's disease can be a sexually debilitating disease resulting in significant psychological stress for many men. Appropriate treatment should be individualised and tailored to the patient's expectations, disease history, physical examination findings and erectile function. Conservative measures should be applied primarily in symptomatic patients with Peyronie's disease. Most men need only reassurance and a watchful waiting approach, because pain will resolve spontaneously and plaque formation usually stabilises with time. Patients with Peyronie's disease and their partners must be educated about what is happening and what might happen. They must be told that in the majority of cases their sexual relationship can be adequately restored. Treatment of men with erectile dysfunction, if present, is also very helpful. Only a limited number of men with Peyronie's disease need surgical treatment because

of severe curvature and associated sexual problems. **MT**

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A list of references is available on request to the editorial office.

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**BENJAMIN DAVIDSON** MB BS(Hons), BSc(Hons), PhD(Biochem) **PETER SUTHERLAND** MB BS, FRACS

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