New Hope For Men With PEYRONIE'S DISEASE

If intercourse has become difficult or painful because your penis curves when erect, you may have a condition known as Peyronie's disease (PD).

In PD, hard nodules, called plaques, form in the sheath surrounding the vascular erectile tissue within the penile shaft. The plaques, which are not cancerous, cause the penis to bend toward the affected side. This can interfere with erection and penetration and reduce penile length, causing much distress for the man and his partner.

The causes of PD are not altogether clear. Fortunately, however, as research into the disease continues, new medical therapies are emerging and surgical techniques are being refined.

In this article, we'll discuss what is known about PD—possible causes, typical signs and symptoms, frequency, and risk. We'll explore some of the myths surrounding the disease, describe the treatments currently in use or under investigation, and discuss which patients are most likely to benefit from the various treatments.

WHAT CAUSES PD?

Much is still unknown about the causes of PD, but research suggests it is a disorder of wound healing. The PD plaques are actually hardened scar tissue. It's widely believed that the disease is triggered by an injury to the erect penis—often one that goes unnoticed by the man. What is unclear is why a relatively minor injury would lead to such excessive scarring.

Normally, wounds heal in three phases: First, enzymes clean the wound of dead or damaged tissue. Second, the body repairs the wound by forming a scar that strengthens the injured tissue. Finally, the collagen fibers that make up the scar are broken down and realigned leaving a smaller "remodeled" scar. In PD, not only is scar formation extreme, but scar remodeling either fails to occur or is insufficient.

The abnormal scarring of PD is believed to be related to the actions of fibrin and cytokines, which stimulate the formation of scar tissue in the second phase of wound healing. It seems that, in PD, these substances allow excessive amounts of collagen to collect. The enzymes protease and

collagenase, which are responsible for remodeling scar tissue in the third phase of wound healing, also may play a role. Patients with PD may produce too few of these enzymes or the enzymes they produce may not function properly to remodel the scar.

Some investigators believe that the tendency to develop PD may be inherited. There is a reported association between PD and a genetic disorder called Dupuytren's contracture, in which scar tissue forms along the sheath surrounding tendons in the palm of the hand, causing the ring finger to contract inward.

SIGNS AND SYMPTOMS OF PD

The plaques of PD develop in the tunica albuginea—the fibrous tissue that covers the penile erection chambers, known as the corpus cavernosa. The plaques restrict penile expansion during erection and cause the erect penis to bend in the direction of the plaques, which are usually on the upper (or "dorsal") surface but may be on the underside (the "ventral" surface) or on either side ("lateral" plaques). Some plaques are so small that they cause only a slight indentation. Others go all the way around the penis, causing the penis to take on an hourglass shape. Generally, the greater the curvature of the penis, the more difficult it is to penetrate during sexual intercourse. Hourglass and indentation deformities can cause sexual difficulty too, sometimes causing the penis to buckle during penetration attempts.

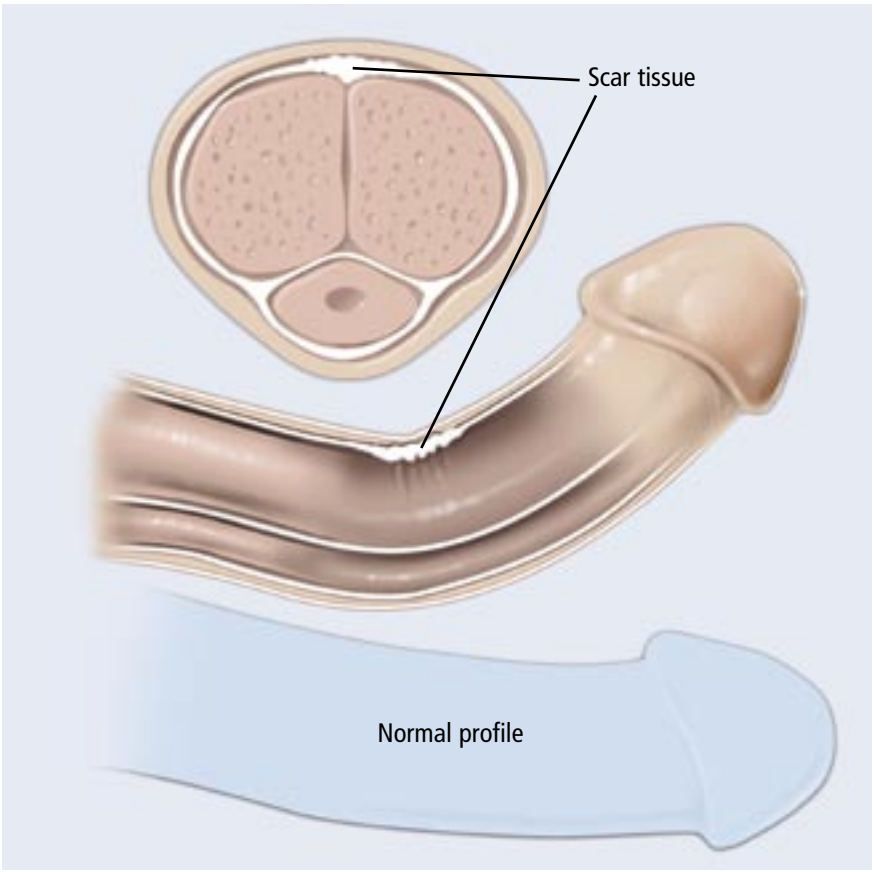
Peyronie's disease may be associated with pain, especially in the initial stages, and with penile shortening. Many men with PD have erectile dysfunction (ED), which means they find it difficult to have an erection or to maintain one long enough to have satisfactory sex.

Contrary to popular belief, in most cases, PD does not get better without treatment. Spontaneous improvement or resolution has been said to occur in anywhere from 3% to 15% of all cases (see "Myths About PD" on page 10).

HOW COMMON IS PD AND WHO GETS IT?

In the late 1990s, PD was thought to be relatively uncommon, with many researchers reporting a prevalence of only 1%. Recent studies, however, suggest that the condition is far more widespread. A 2004 survey of 534 men undergoing urologic examination at prostate cancer screening centers revealed that nearly 9% had signs of PD.

Typically, PD is diagnosed in middle-aged men, though it can occur in men of any age, from adolescence onward. Although it tends to occur most frequently in Caucasians, men of any ethnic group may develop PD.



MYTHS ABOUT PD

MYTH	FACT
Peyronie's disease (PD) is rare	PD occurs in nearly 1 in 10 men
PD is a disease of older men	PD can occur in men of any age
PD usually resolves spontaneously	Most cases of PD require treatment; only 3% to 15% of all cases improve or resolve spontaneously

PILLS FOR PD

Researchers have studied a number of oral therapies for PD, including: carnitine, colchicine, potassium aminobenzoate, tamoxifen, and vitamin E, the first oral therapy used for PD was believed to be of value because of its antioxidant properties. The other oral agents were studied because they are thought to have properties that interfere with collagen synthesis and scar formation.

Unfortunately, most studies using oral PD therapies haven't been well controlled. Since some PD cases improve on their own and few studies of oral medication have compared treated patients to an untreated "control group," it's not clear that the oral therapies for PD offer any benefit over no treatment at all in terms of penile curvature, pain, or the ability to have intercourse. The active phase of Peyronie's disease takes 12 to 18 months. After this pain generally goes away but most patients are left with a penile nodule/plaque. The Peyronie's plaque causes bending and shortening of the erection.

IS PD SURGERY RIGHT FOR YOU?

If you can answer "yes" to the following questions, you may want to discuss surgical options with your doctor:

1. **Have you had Peyronie's disease (PD) for more than one year?**
2. **Is your PD stable (meaning symptoms have not changed for six months or more) and painless?**
3. **Does PD prevent you from engaging in satisfactory sex, or are your PD plaques calcified (made inflexible by calcium deposits)?**

INTRALESIONAL INJECTION THERAPY

Several agents have been studied as intralesional injection therapies, meaning that they're injected directly into the PD plaques, or lesions. Some of the earliest drugs used in this way were steroids. Currently, intralesional steroid injection is discouraged in the treatment of PD because there are no clear benefits, it can cause penile tissue to atrophy, or waste away, and it can complicate subsequent surgery.

Verapamil, a calcium channel blocker usually used to treat high blood pressure, has been shown to stop collagen synthesis and increase collagenase activity, thereby promoting scar remodeling.

Likewise, interferon injections have been associated with PD improvement. In placebo-controlled studies, documented benefits have been established. Interferons work by increasing collagenase and reducing collagen formation.

TOPICAL GEL THERAPY

Verapamil was introduced as a topical gel in the mid 1990s. It was hoped that the drug, which had been somewhat successful as an intralesional injection, could produce the same results with less discomfort in this noninvasive form. Unfortunately, when applied topically, the drug fails to reach the tunica albuginea. This was confirmed when men scheduled to undergo penile prosthesis surgery had verapamil gel applied to the penile shaft the night before and morning of surgery. During surgery, small tissue samples from each man's tunica albuginea were removed and examined for verapamil. No verapamil was detected in any of the sampled tissue.

IONTOPHORESIS

The process of iontophoresis, also known as electromotive drug administration or EMDA, uses an electric current to administer a drug through intact skin. In the treatment of PD, this technique has been used to administer vera-

UNDERSTANDING THE RISKS OF PD SURGERY

All surgery caries risks, and Peyronie's disease (PD) surgeries are no exception. Before undergoing surgery, be sure you understand the following potential risks—and discuss them with your doctor.

- **Reduced penile rigidity (firmness)**
- **Diminished penile sensation and delayed ejaculation, a problem that may not resolve for up to six months after surgery**
- **Shortening of the penis**
- **Persistent or recurrent curvature, which is unusual if the PD is stable before surgery**
- **Delayed resumption of sexual activity (sometimes up to six months after surgery)**

pamil—with or without the steroid dexamethasone—through a fluid-filled reservoir affixed to the penile skin overlying the plaque sites. Early investigation found the treatment effective in reducing pain, plaque size, and penile curvature. Furthermore, measurable levels of verapamil have been found in tunica albuginea samples taken from men undergoing surgery for penile straightening and plaque removal.

ELECTROSHOCK WAVE THERAPY

Electroshock wave therapy has been tested as a means of breaking up PD plaques, promoting plaque resorption, improving blood flow to the penis, and straightening the penis. To date, no consistent improvements in penile curvature, plaque size, sexual function, or rigidity have been reported with this treatment.

SURGERY

Men who have had PD for more than one year, are unable to have satisfactory sexual intercourse, and whose PD is painless and stable may be candidates for PD surgery (see "Is PD Surgery Right for You?" on page 10). Surgery is still the "gold standard" for correcting penile curvature associated with PD, and surgical technique has improved tremendously over the past several years.

No one type of surgery is right for all patients. If you can maintain a satisfactory erection (with or without medication), the curve in your penis is less than 60 degrees, and your penis has neither an hourglass nor a hinge deformity, your doctor may recommend tunica albuginea plication. When plication is performed, the tissue of the tunica albuginea on the opposite side of the plaque is plicated, or stitched, to counteract the bending effect.

If your penis has more severe curvature, or if there is severe narrowing in your penile shaft so that it cannot become erect without buckling, then a more complex surgery is required: plaque incision and grafting. This requires the plaque to be incised (cut into), straightened, and filled in with a graft, which is either composed of living tissue from another part of your body or harvested from human or animal tissue.

If postsurgical erections are unsatisfactory, treatment with Cialis, Levitra, or Viagra may be prescribed to enhance erectile response.

Prosthetic surgery (a penile implant) was once the mainstay of PD therapy. Today, that type of surgery is performed only on patients with PD and ED. Plaque excision (removal) is reserved for men with severe calcified PD.

All PD surgeries carry potential risks, including incomplete straightening, ED, and diminished penile sensation. Before undergoing any type of PD surgery, be sure to discuss all risks thoroughly with your doctor (see "Understanding the Risks of PD Surgery" on page 10).

In most cases, surgical correction of PD successfully straightens the penis and makes it more rigid, but in the early phases of PD, other approaches are usually tried first. If you have signs and symptoms of PD, talk to your doctor about what treatment is best for you. □

PD PATHOGENESIS AND NATURAL HISTORY

Microtrauma to penis

- Up to 40% remember vital injury
- In 20% onset is sudden

Injury to tunica albuginea (TA)

- Possible bleeding between layers
- No bruising at skin is evident

Wound healing process is:

- Dysregulated
- Proliferative
- Permanently changes elastic fibers of TA

Pain with erection (6-12 months)

Plaque/nodule

Penile bend, deformity, or shortening

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