Priapism

A Melman1* and S Serels1

1Department of Urology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York, USA

Priapism is a prolonged, painful, penile erection that fails to subside despite orgasm. An erection lasting longer than 4–6 h is considered to be priapic; nevertheless, pain does not usually ensue until 6–8 h have elapsed. Priapism is considered a failure of the detumescence mechanism, which may be due to excess release of contractile neurotransmitters, obstruction of draining venules, malfunction of the intrinsic detumescence mechanism, or prolonged relaxation of intracavernosal smooth muscle. There are essentially two main types of priapism: high flow (non-ischemic) and low flow (ischemic). Low flow priapism is the more common form, and it is associated with a decrease in venous outflow and vascular stasis that, in turn, cause tissue hypoxia and acidosis. This form of priapism is usually quite painful because of tissue ischemia. Penile blood aspirated from cavernous spaces appears dark in color. Immediate treatment is necessary or penile fibrosis will ensue. High flow priapism is usually due to trauma, although, on rare occasions it has been idiopathic or due to sickle cell disease. The hallmark of this type of priapism is an increase in arterial inflow in the setting of normal venous outflow. Aspirated penile blood is noted to be bright red and has a high \( pO_2 \). This form of priapism is not usually painful because it is non-ischemic. Treatment is dependent on the wishes of the patient but is not mandatory.

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Introduction

Normal physiology of erection

Erection is a vascular event and the penile corpora are specialized vascular beds of endothelial-lined sinusoidal spaces supported by a framework of smooth muscle, collagen, nerves, nutritive arterioles and capillaries. Normal erectile function is a complex interaction of both the nervous and vascular systems. The arterial supply to the penis is from the internal pudendal artery, a branch of the internal iliac artery. As classically represented, this artery trifurcates into the dorsal, cavernous, and urethral arteries. Each of the paired cavernous arteries enters the hilum of the penis where the two crura merge. The cavernous artery lies close to the septum at the penile base and becomes more centrally located in the mid and distal penis. Throughout the course of the penile portion of the corpora cavernosa, the cavernous arteries give off helicine arterial branches that supply the trabecular erectile tissue and sinusoids. The crural sinusoidal spaces are fed by retrograde flow from the more distal helicine branches of the cavernous artery that enters the penis at the level of the pubic synthesis. The urethral artery supplies branches to the corpus spongiosum and the glans penis while the bulbar artery supplies the bulbar urethra as well as the bulbospongiosum muscle. The dorsal artery, which lies under Buck’s fascia, also supplies the glans penis. The venous drainage originates from the small venules derived from inside the trabeculae between the tunica and peripheral sinusoids. The blood then exits the tunica albuginea via the emissary veins and returns to the circulation by two main channels: the cavernous vein and the deep dorsal vein. The cavernous veins are primarily responsible for the drainage of the corpus cavernosum.

Erection requires relaxation of trabecular smooth muscle that results in increased compliance of the sinusoids and arterial wall as well as dilation of the arterioles and arteries. As a result of the arterial engorgement that occurs with smooth muscle dilatation, there is: (i) passive trapping of incoming blood by expanding sinusoids; (ii) compression of the subtunical venous plexuses in the trabeculae between the tunica albuginea and the peripheral systems.
sinusoids which reduces venous outflow; and (iii) stretching of the tunica albuginea to its capacity which encloses the emissary veins between the tunical layer and decreases venous outflow.

In the flaccid state, the helicine arteries are contracted and tortuous. At this time the blood is shunted to the trabecular framework, and the rate of blood flow to the entire penis is 3–5 ml/min. Only a small fraction of that flow enters the sinusoidal spaces. The remainder percolates through the trabeculae and nourishes its tissues. Furthermore, despite the fact that the metabolic rate of the corporal smooth muscle has not been reported, the penis is an external organ with a lower than central body temperature and therefore its energy needs can be met at very low blood flow rates. During sexual excitement, the helicine arteries dilate and straighten which in turn allows blood to enter directly into the sinusoidal spaces. At that time, there is a 5–10 fold increase in blood flow to the penis. Needle aspiration of blood from the sinusoidal spaces during normal erection has a PO2 of approximately 40 mm Hg, a PCO2 of 40 mm Hg, and a pH of 7.4.

The innervation to the penis is what triggers relaxation of the arterial smooth muscle. The cavernosal nerves arise from the pelvic ganglionic plexus, found in the retroperitoneum adjacent to the rectum. This plexus is composed of parasympathetic nerves arising from S2–S4 as well as a sympathetic contribution from the hypogastric plexus. The parasympathetic nerves were historically thought to be responsible for tumescence while the sympathetic system facilitated detumescence. Non-adrenergic non-cholinergic (NANC) nerves are responsible for the relaxation of the arterial and cavernosal smooth muscle. These NANC nerves stimulate the release of vasodilating neurotransmitters such as nitric oxide that relaxes the smooth muscle via an increase in cGMP.1,2

**Definition and description of priapism**

Priapism is a malfunction of the normal detumescence mechanism. It is defined as a prolonged penile erection that fails to subside despite orgasm. An erection lasting longer than 4–6 h is considered to be priapic. Priapism is a failure of the detumescence mechanism which may be due to excess release of contractile neurotransmitters, obstruction of draining venules, malfunction of the intrinsic detumescence mechanism, or prolonged relaxation of intracavernosal smooth muscle.

There are essentially two main types of priapism: high flow (non-ischemic) and low flow (ischemic). Low flow priapism, the more common form, is associated with a decrease in venous outflow and vascular stasis that causes tissue hypoxia and acidosis. Pain is associated with low flow, but not high flow, priapism. It is painful because of tissue ischemia. The causes of low flow are multiple and will be discussed below. Low flow priapism generally affects the corpora cavernosum with preservation of blood flow in the glans and corpus spongiosum; however, tricorporal priapism has been described in sickle cell patients.3,4

High flow priapism is usually a result of trauma though it may occur in men with sickle cell disease. The hallmark of this type of priapism is an increase in arterial inflow in the setting of a normal venous outflow. Aspirated penile blood is noted to be bright red and have a high PO2. This form of priapism is not usually painful and is non-ischemic.

**Classification of low flow priapism**

**Hematologic/thrombotic causes**

Sickle cell patients commonly experience episodes of priapism because of the sickled red blood cells impeding the outflow of penile blood flow. Two recent retrospective studies showed that 38–42% of men with sickle cell disease have at least one episode of priapism in their lifetime.5,6 Approximately 23% of adult cases and as many as 63% of pediatric priapism are a result of sickle cell disease.7 Furthermore, although this is normally a low flow priapism, there have been several reports of high flow priapism in sickle patients for unknown reasons.7,8 It has been hypothesized that high flow sickle priapism may result from a failure of the autonomic regulation.9 Leukemia is the cause of less than 1% of all priapism. This form of priapism is most commonly seen with chronic granulocytic leukemia. Patients with this type of leukemia have a 50% chance of having priapism; fortunately, chronic granulocytic leukemia accounts for only 5% of pediatric leukemias.10,11 The etiology of this type of priapism is not known, but it is hypothesized that leukemia may result in hyperviscosity and sludging due to the increased number of white blood cells.

Total parenteral nutrition which contains 20% fat emulsion has also been noted to cause priapism. It is thought that this occurs due to an increase in blood coagulation.12–14 This increased coagulation may be due to a distortion in erythrocyte morphology which in turn results in an increase in adhesiveness. There are others who believe that priapism in this setting is simply due to embolization of fat.13,14

**Oral medications**

There is a well known association between certain medications and priapism, the most common being...
antidepressants, antipsychotics, and antihypertensives. Trazodone is the antidepressant that causes priapism most often. The mechanism is thought to be secondary to alpha-adrenergic blockade. Chlorpromazine, a phenothiazine, and clozapine, an atypical antipsychotic, have been reported to cause priapism. There are also several antihypertensives such as hydralazine, prazosin, guanethidine which have been associated with priapism. Furthermore, heparin and cocaine abuse, though less frequent, have also been reported to cause priapism.

Intracavernous injection therapy

Intracavernous injections have been used for the treatment of erectile dysfunction since 1982 when Virag introduced papaverine as a means of inducing erections. Excessive dosing with intracavernous agents can result in priapism, and today, it is the most common cause of this problem. The incidence of priapism appears to be lower with prostaglandin E1 than with papaverine alone or papaverine combinations. The lower incidence of priapism with prostaglandin E1 is thought to be due to the presence of enzymes in the penile tissue that can metabolize it.

Metastatic lesions

Common primary cancers that can metastasize to the penis and result in priapism are bladder (30%), prostate (30%), rectosigmoid (16%), and renal (11%). This phenomenon is believed to be due to an obstruction of the venous outflow by the tumor and should always be considered as a possible cause of priapism in an individual with a history of carcinoma.

Neurologic

Individuals who have suffered spinal cord injuries, especially high cord lesions, are also prone to experience priapism. This form of priapism is usually self-limiting and does not require intervention. In addition, Baba et al. have reported on several cases of intermittent priapism associated with spinal stenosis.

Idiopathic

Thirty to fifty percent of all priapism events are considered idiopathic. Most of these events are considered to be low flow.

Classification of high flow priapism

The most common cause of high flow priapism is penile or perineal trauma which results in a cavernosal artery to corporal tissue fistula. Furthermore, there are several reports of idiopathic high flow priapism, and as mentioned previously, there are a few cases of high flow in association with sickle cell disease in the absence of trauma. The term high flow priapism, though identified in case reports as early as the 1960s, was not clearly defined until 1983 by Hauri et al. This entity is due to an increase in arterial flow which is not regulated by the helicine arteries and does not activate the veno-occlusive mechanism. Thus, blood flows in and out at incredible rates. There is a paucity of reported cases of documented high flow priapism. Bastuba in 1994 commented that there are only 16 cases of angiographically proven high flow priapism which supports the rarity of this entity.

Evaluation of priapism

As with any patient evaluation, a good history is needed to identify any previous conditions, drug use, or recent trauma. Performing a physical exam is also essential, and through these means, one may find an abdominal mass, enlarged lymph nodes, or signs of trauma. It is also important to note that in a low flow priapism, the glans penis is usually soft while the corpus cavernosum are 100% rigid. In contrast, high flow priapism usually causes 60–100% rigidity. Laboratory tests, including a complete blood count and perhaps a sickle prep or electrophoresis should be performed when applicable. In order to distinguish high from low flow priapism, visual inspection is helpful, and blood can be aspirated from the corpora cavernosum and sent for blood gas analysis. Blood gas values of pH < 7.25, Po2 < 30, and PCO2 > 60 have been suggested to represent ischemic or low flow states. Furthermore, Doppler evaluation can be helpful in confirming high flow priapism by showing increased arterial flow in one or both cavernous arteries. In addition, angiography can be performed to establish the diagnosis of high flow priapism but is not essential.

Therapy for low flow priapism

In low flow priapism, it is important to treat the patient expeditiously by increasing the outflow of cavernous blood. In just 24 h, endothelial and trabecular destruction have occurred, and by 48 h, widespread smooth muscle necrosis has taken
place. The natural sequelae of untreated ischemic priapism is penile fibrosis and impotence. The treatment of this type of priapism depends on the etiology. Priapism that is caused by metastatic disease is usually indicative of advanced disease as well as a short life expectancy and is therefore treated expectantly. If leukemia is the cause of priapism, chemotherapy and/or radiotherapy is recommended.

Sickle cell priapism is usually treated with medical therapy. The mainstay of therapy is hydration, alkalinization, analgesia, and hypertransfusion. The use of hypertransfusion is performed so as to increase the hemoglobin concentration to greater than 10 mg/dl and reduce the hemoglobin S to less than 30%. If these conservative measures are ineffective, then corporeal aspiration and instillation of alpha adrenergic agents can be attempted. Furthermore, the use of surgery is considered a last resort and is rarely used. Some believe that the conservative measures work better in high flow states than in low flow because irreversible ischemia is not occurring. In a recent review by Miller et al. of 400 pediatric patients with sickle cell priapism with an age range of 5–19 y, only eight patients sought medical evaluation for priapism. Four of the eight were noted to have low flow priapism. Two of the four patients had resolution of their priapism with conservative measures while the other two required surgery. Out of the four patients with high flow priapism, three improved with conservative therapy. Virag et al. described the use of an oral alpha-adrenergic agent, etilefrine, as a preventive measure in association with intracorpororeal injection therapy for acute episodes. There is also a case report of hydralazine being used to treat sickle cell priapism though this therapy requires further investigation.

For all other types of low flow priapism, it is acceptable to try corporal aspiration of blood with irrigation with non-heparinized saline as a first line therapy. If the priapism still persists, the corpora can be irrigated with an alpha-agonist. Most urologists like to use phenylephrine at a dose of 100–200 µg/0.1 ml. This dose can be repeated several times at approximately 5 min intervals. Phenylephrine is a relatively pure alpha-1 adrenergic agonist with minimal beta-adrenergic activity. The use of metaraminol has been essentially abandoned due a reported death from its use. Table 1 shows the preparation of dilutions of alpha-adrenergic agonists which are useful for the treatment of priapism.

Stilbesterol and gonadotropin-releasing hormone (GNRH) analogues have been tried for the chronic treatment of recurrent sickle cell priapism. Steinberg and Eyre have reported on the use of epinephrine self-injection therapy in association with monthly intra-muscular GNRH to treat sickle cell priapism. Ironically, GNRH has also been associated with priapism. Similarly, an antiandrogen such as CasodexTM or FlutemideTM can be administered. Enhancement of smooth muscle tone can be achieved with sustained-released alpha3 agonist administration that is usually packaged along with an antihistamine. Glycopyrrolate was reported to reduce intra-operative priapism and may be considered useful when cardiovascular stability is desired, and/or the use of alpha-agonists are prohibited. Thus, the exact role of oral and parenteral drug therapy for priapism has yet to be completely determined, but studies are ongoing. Surgical therapy is always an option if all attempts at conservative treatment have failed. The goal of surgical therapy is to provide a shunt between the corpus cavernosum and either the glans penis, the corpus spongiosum, or a vein so as to bypass the obstructed veno-occlusive mechanism. This can be performed in a variety of methods as shown in Table 2.

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**Table 1** Dilutions of alpha-adrenergic agonists used to treat priapism

| Drug         | Dosage (intermittent injection) | Alpha-adrenergic activity | Beta 1-adrenergic activity | Beta 2-adrenergic activity |
|--------------|---------------------------------|---------------------------|---------------------------|---------------------------|
| Ephedrine    | 50–100 mg                       | +                         | +                         | +                         |
| Epinephrine  | 10–20 µg                        | + +                       | + +                       | + +                       |
| Metaraminol  | 2–4 mg                          | +                         | +                         | +                         |
| Phenylephrine| 100–200 µg (10 doses max.)      | + +                       | –                         | –                         |
| Norepinephrine| 10–20 µg                     | + +                       | +                         | +                         |

**Table 2** Shunt procedures in priapism

| Type of shunt                  | Description                                                                 |
|--------------------------------|-----------------------------------------------------------------------------|
| Winter shunt (caverno-glanular shunt) | Percutaneous shunt with tru-cut needle from glans to tip of corpus cavernosum |
| Al-Ghorab (caverno-glanular shunt) | Formal incision at corona and removal of corporal tips = > communication between glans and corpora |
| Quakles (caverno-spongiosal shunt) | Formal surgical anastomosis of corpus cavernosum with proximal corpus spongiosum |
| Grayhack (caverno-saphenous shunt) | Anastomosis of corpus cavernosum with saphenous vein |
| Caverno-penile dorsal vein shunt | Anastomosis of corpus cavernosum with dorsal vein |
The caverno-glansular shunts are usually the first to be performed due to their technical ease and low morbidity. If these shunts fail then the Quakles shunt is attempted. This shunt should be performed as proximally as possible where the corpus spongiosum is thickest so as to avoid injuring the uretha. The Grayhack and the caverno-penile dorsal vein shunt are more difficult technically and have been associated with pulmonary emboli. Therefore, these two shunts are usually not performed.

The problem with surgical therapy is that there is a high rate of impotency (ca 50%), and for this reason, it is only used after conservative methods have failed. One can assess the need for formal shunt surgery with an angiograph test. In this test, an angiocath 18-gage needle is placed in the turgid corpora. If blood can be expressed, it signifies that cavernous edema is minimal and that a shunting procedure will be of value. If no blood drains, then formal surgery will be of no avail. Impotence will occur from the events of prolonged untreated priapism. The considerable fibrosis that ensues is best treated with a penile prosthesis so that the man can resume coitus.

**Therapy for high flow priapism**

High flow priapism is not considered an emergency. The penis is not ischemic, and potency has been maintained even if priapism exists for months. Therefore, observation has been considered as an option with the hope of spontaneous detumescence. Methylene blue which blocks the effect of nitric oxide has been tried in high flow states that are not due to cavernosal artery injury with some success, but its use is discouraged because of the possibility of penile necrosis and formation of necrotic abscesses. High flow priapism in the case of sickle cell disease is best treated with conservative measures in the same manner as low flow sickle cell priapism. Shunt procedures have also been tried in those patients refractory to conservative therapy. In addition, Ramos et al reported the successful use of bilateral pudendal artery ligation for this condition.

The more definitive therapy for high flow priapism which is due to penile or perineal trauma or in certain idiopathic cases is either cavernosal artery ligation or embolization. Embolization is usually recommended and surgery is reserved for failures. Autologous clot and absorbable gelatin sponges have been advocated for embolization because they permit rapid return of blood flow after clot lysis and thereby minimize complications. In a report by Bastuda et al, six patients were embolized and all recovered erectile function. Nevertheless, all patients undergoing this type of intervention should be aware of the possibility of impotency. Other than impotency, there are few complications reported after selective embolization. There is, however, a report in the literature of a perineal abscess after embolization.

**Conclusion**

Priapism can be quite debilitating and result in serious sequelae. There are essentially two broad categories of priapism (ie high flow and low flow). Low flow priapism is much more common and can be caused by hematologic disease states, oral medications, intracavernous injection therapy, metastatic disease, and neurologic causes. This type of priapism may also occur idiopathically. High flow priapism on the other hand is more likely to be due to trauma although it can also be idiopathic or associated with sickle cell disease. Low flow priapism is considered a urologic emergency and should be treated promptly while high flow treatment is not an emergency. The treatments for all types of priapism are initially conservative but surgical therapy is available when applicable. The problem with surgical intervention for this disease which affects so many young sexually active individuals is that the impotence rates are high. At this time, there is no good oral/parenteral therapy available for all types of priapism.

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Appendix

Open discussion following Dr Melman’s presentation

Dr Morales: How confident are you with the angiocath test?

Dr Melman: We’ve only done it twice, so this is a very small ‘n’, but then you open these patients who have sustained edema, you don’t get any blood flow from the corporal bodies. If you actually do the surgery, you see just totally edematous cavernous bodies, so I’m reasonably confident.

Dr Wessells: I would beg to differ; the more distal you are on the penis, the more edema there is. And I have done some proximal shunts at the bulbospongiosus level and gotten good blood flow where I can’t aspirate anything out of the distal end.

Dr Melman: Not aspirate. You put in an open catheter, and let it drain to gravity; it’s not aspiration. If you’re aspirating, it’s difficult because you’re sucking tissue up against the end of the catheter.

Dr Mulcahy: Has anybody ever seen a patient whose erections would rise again after three or four days of rock-hard priapism?

Dr Melman: Maybe not, but what about at 48 hours? At least it gives you some clue as to whether or not you’ll get some blood flow into the shunt itself. At four days it wouldn’t make a difference.

Dr Lewis: We just do not know how to treat sickle cell priapism. Nobody with sickle cell priapism beyond 12 hours does well. I’ve been reluctant to try phenylephrine because of the theory that you can cause more arterial constriction and perhaps produce greater priapism but some have had success types of priapism. There is the pharmacological agent-induced low flow. There’s a sickle cell low-flow that’s very much like idiopathic. And then there’s a stuttering priapism.

Dr Pryor: What do you think about the patient with a 72-hour erection that you can’t get down? Would you consider prophylactically putting a prosthesis in? The problem is, if you wait, it gets scarred and the prosthesis is harder to put in.

Dr Melman: I would wait, and be sure to tell the patient that they’re going to get scarring. Later on, when the disease is resolved, we’ll treat it.

Dr Lewis: From a medical/legal standpoint, when you begin treatment of priapism in all patients, you should inform both the patient and the parents who have sickle cell disease children, that the damage is already done. Chances are, with or without treatment, the outcome is going to be the same.

Dr Melman: Does anyone have other suggestions for oral medication to prevent stuttering priapism and priapism in sickle cell disease? I understand from Dr Goldstein that digoxin doesn’t work.

Dr Lewis: When you could still get low-dose estrogen, I used it in a number of patients with stuttering priapism and it worked. LHRH agonists and estrogen together really control the stuttering priapism.

Dr Melman: You’re eliminating the REM erections and hypogonadal men don’t get REM erections. Casodex and Flutamide do the same thing.