IMPOTENCE

Part of "42 - THE PENIS: SEXUAL FUNCTION AND DYSFUNCTION"

Etiology

Various diseases have been associated with impotence. In many instances, a cause-and-effect relationship has not been demonstrated; in other instances, clinical observations have significantly contributed to our understanding of both erectile physiology and impotence. Causative processes are categorized as follows: (a) neurologic disorders, (b) vascular disorders, (c) endocrine disorders, (d) surgical and traumatic disorders, (e) drug-associated erectile dysfunction, and (f) psychogenic erectile dysfunction (346).

Neurologic Disorders

Neurologic causes of impotence can be viewed most conveniently as peripheral neuropathy, spinal cord lesions, or lesions of the cerebral hemispheres.

Peripheral Neuropathy

Diabetic Neuropathy.

Diabetes mellitus is a common cause of impotence. This was first suggested as long ago as 1798 by Rollo (100). Diabetes has a profound effect on the vascular system, causing accelerated atherosclerosis and microangiopathy. This microangiopathy particularly affects the eyes, kidneys, and central and peripheral nervous systems. The incidence of impotence in diabetic men increases with age. In a study involving 198 diabetic men, impotence occurred in 7.5% of patients younger than 45 years of age, 23.2% at 50 years of age, 40.2% at 60 years of age, 58.4% at 70 years of age, and 80% at 80 years of age (295). These figures are two to five times higher than those found in healthy control subjects (39). The clinical course of impotence in diabetic men is most often gradual, beginning with decreased firmness or rigidity and progressively worsening.

The erectile abnormality associated with diabetes is thought by some to be primarily a neurologic rather than a vascular or endocrinologic problem. Ellenberg (90) identified peripheral neuropathy in 38 of 45 impotent diabetic patients, but others (226) have found a much lower incidence of neuropathy associated with impotence. Impotent diabetic men often have a peripheral neuropathy with diminished or painful sensation, muscle wasting and weakness, and trophic changes of skin and joints (39). However, impotence may be the first and only symptom of diabetes. Deutsch and Sherman (78) reported that up to 12% of impotent men have unrecognized diabetes mellitus. Masters and Johnson (227) suggest that there is a 200% to 300% higher incidence of abnormal glucose tolerance tests in men with impotence than in a representative cross section of the population. They also emphasize that careful maintenance of medical control often does not reverse the impotence once developed. Recent evidence suggests that the prevalence of impotence is lower in diabetic men who maintain good control of blood sugar, as measured by

hemoglobin $A1_c$ (285). Libido is often preserved but may lessen as a result of frustration and other psychologic factors that occur because of lifestyle changes secondary to chronic disease. Impotence associated with diabetes cannot be assumed to be purely organic; psychologic factors also deserve attention.

The neuropathic changes associated with diabetes have long been considered one of the main causative factors in diabetic impotence. Somatic and autonomic neuropathy are more common in impotent than in nonimpotent diabetic men (54). A proportion of these patients complain of orthostatic hypotension and difficulty with micturition (91). Studies using instantaneous heart recordings have demonstrated that the onset of autonomic dysfunction may occur without evidence of peripheral neuropathy and may precede symptoms of autonomic dysfunction by a number of years (217). The association of autonomic neuropathy with diabetes mellitus is still not clear. Fairburn and colleagues (98) found no difference in cardiovascular autonomic neuropathy in impotent versus potent diabetic men. Ewing and associates (95) studied the vascular reflexes in 31 males with autonomic neuropathy. Of this group, 28 complained of impotence, and it was an isolated problem in 15. Vascular reflexes were studied by recording heart rate changes during the Valsalva maneuver and by measuring blood pressure response to sustained hand grip. Patients with abnormal vascular reflexes had greater evidence of peripheral neuropathy as measured by nerve conduction studies. There was a notable difference in responses of patients with impotence alone and the patients with other features of autonomic neuropathy with or without impotence. The vascular reflexes were less abnormal in those patients whose only manifestation of autonomic neuropathy was impotence. These investigators concluded that only when impotence is associated with other features of the disorder can it be attributed to autonomic neuropathy. Thus, if impotence is the only suggestion of autonomic neuropathy in the diabetic patient, other possible causes of sexual dysfunction should be sought.

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Abnormalities of the sacral reflex in diabetic patients have been demonstrated by cystometric findings (90) and lengthened bulbocavernosus reflex latency times (156). Neuromorphologic changes can be seen by microscopic examination of the autonomic nerve fibers of the corpora cavernosa in impotent men (97). Ellenberg (91) reported the cystometric findings in 45 diabetic men who complained of impotence; only 8 had normal findings. The other 37 patients had increased bladder capacity (greater than 500 mL); 6 had residual urine with no cystoscopic evidence of bladder neck obstruction. Five of the diabetic patients had neither cystometric abnormalities nor involvement of the peripheral nervous system. Ellenberg concluded that impotence was psychogenic in 4 of these 5 patients as “indicated by the presence of morning erections and competence in extramarital situations in two and intermittent impotence in two.” Of note, only 3 of 30 diabetic patients without the complaint of impotence had abnormal cystometrograms (91).

Despite the fact that many accept autonomic neuropathy as the underlying disorder in impotent diabetic men, vascular factors may play an important role. Vascular changes in diabetic patients resulting in retinopathy and neuropathy are well known. These vascular lesions have been associated with impotence in the diabetic male (145). Ruzbarsky and Michal (298) reported on the morphologic changes in the arterial bed of the penis associated with aging. Microangiopathy occurred 10 to 15 years earlier in the diabetic man

than in the nondiabetic man.

With Doppler studies, cystometrograms, and bulbocavernosus latency tests, Jevitch and associates (156) compared the vascular and neuropathic changes in a group of impotent diabetic men. Vascular obstructive changes occurred in 95% of the patients; 72% were severe and 23% mild. Abnormal neurologic studies were noted in only 34%. All of the patients with neurologic changes also had vascular abnormalities. In addition, 98% of the impotent diabetic men had normal antegrade ejaculation.

Hormonal abnormalities do not appear to play a prominent role in the sexual dysfunction of diabetic patients. In the prospective study by Ficher and colleagues (100), serum levels of testosterone, prolactin, LH, and follicle-stimulating hormone (FSH) were not significantly different in impotent diabetic patients when compared with impotent nondiabetic patients.

Uremic Neuropathy.

Patients with chronic renal failure, particularly those undergoing dialysis, are frequently impotent, with complete impotence noted in 20% to 60% of patients (67). Even though uremic neuropathy may contribute to impotence, the hormonal abnormalities associated with uremia may play the predominant role (67). Holdsworth and colleagues (150) found significant elevations of LH and FSH in uremic patients. Serum testosterone levels were subnormal. Histologic examination of testes biopsy samples revealed severe spermatogenic damage. Bailey (11) concluded that testicular suppression was a result of the cellular toxic effects of retained uremic toxins. A more detailed discussion follows in the section describing endocrine causes of impotence. In addition to the neuropathy and endocrinopathy associated with uremia, the vascular effects of uremia have been studied objectively (165). Cavernous artery occlusive disease was found in 78% of patients with chronic renal failure. In addition, corporovenous leakage was found in 90% of these patients.

Amyloidosis.

Amyloidosis with involvement of the autonomic nervous system can cause impotence. Neurogenic impotence appears to be particularly prominent in heredofamilial amyloidosis. Thus amyloidosis should be included in the causes of male sexual dysfunction. The clinical course of amyloidosis is slowly progressive, and patients usually die in renal failure. No specific therapy exists for amyloidosis (65).

Spinal Cord Lesions

Spinal Cord Injury.

In 1960, Bors and Comarr (41) published their now classic study on sexual function in a large group of patients with spinal cord injuries. The degree and type of sexual dysfunction depend on the level and completeness of the cord lesion. Bors and Comarr found that 94% to 100% of men with upper motor neuron lesions that were incomplete maintained some erectile activity. These lesions may interfere with psychogenic erections, but spontaneous erections and reflex-stimulated erections are common (39). Lower motor neuron or lumbar

spinal cord lesions produce a different clinical picture. Reflex-stimulated erections are absent, but psychogenic erections occur in up to 90% of patients (39,41) with incomplete lesions and in 27% with complete lesions. In a more recent study, Comarr (66) reported 20 patients with complete lower motor neuron cord lesions. Eight patients could obtain psychogenic erection, but none had reflex-stimulated erections. Seven had successful intercourse, and five achieved ejaculation with orgasm. It has been suggested that these phenomena are mediated by means of the sympathetic nervous system because those preganglionic fibers leave the spinal cord at the lower thoracic and upper lumbar level (39). Complete lesions of the sacral spinal cord have the worst prognosis with reference to sexual function. In Piera's study (273) of 100 patients with spinal cord injuries, the 15 patients with complete lesions of the sacral cord had no erections and no ejaculation.

Sexual function is a major concern of patients with acute spinal cord injuries, and physicians should be cautious about predicting the clinical outcome early in the patient's course. Spinal shock with complete or almost complete absence of reflex activity below the level of the lesion commonly occurs (6). Genital reflexes and rectal sphincter activity are profoundly depressed. This may last for many weeks. Thus, before prognosticating, the physician should wait until spinal shock is reversed so that the level and

completeness of the spinal cord lesion can be assessed, thereby allowing for a more accurate prediction of the patient's future course.

Multiple Sclerosis.

Multiple sclerosis is characterized by loss of myelin in the white matter of the brain, brainstem, and spinal cord. Its effect on potency is variable. Vas (349) reported 37 patients between 18 and 50 years of age. Forty-three percent were either totally or partially impotent. Cartlidge (59) reported that 7 of 20 patients with multiple sclerosis were impotent. The severity of the impotence was directly related to the duration of the disease, but in several patients, sexual potency tended to remit and relapse. Sacral-evoked response measurement has been recommended in the evaluation of impotence associated with multiple sclerosis (128). In a comprehensive study of 41 men with multiple sclerosis, sexual dysfunction was present in 29. Of these 29, 8 patients had prolonged sacral latency times. The authors concluded that abnormal sacral-evoked responses may imply neurogenic impotence. In this study, the authors also observed patients with a combination of abnormal perineal electromyography, abnormal sacral latency, and bladder detrusor hyperreflexia, which suggests spinal cord dysfunction at multiple levels.

Other Spinal Cord Diseases.

Other spinal cord lesions that can affect potency include syphilis (tabes dorsalis), spina bifida, syringomyelia, amyotrophic lateral sclerosis, and compression from a herniated disc or tumor (346). Lateral cordotomies used to treat intractable pain also may result in impotence.

Idiopathic orthostatic hypotension (i.e., idiopathic autonomic insufficiency) is often referred to as *Shy-Drager syndrome.* This rare degenerative disorder of unknown cause is progressive, resulting in severe debility and death within 5 to 10 years of onset. It affects

primarily middle-aged men, causing symptoms of autonomic dysfunction, such as loss of sweating, sphincter disturbances, orthostatic hypotension, and impotence (38).

Lesions of the Cerebral Hemispheres

Little information is available concerning the association of cerebral lesions and sexual potency. Frontal lobotomy, Parkinson's disease, Huntington's chorea, and electroshock therapy all may affect libido, but the effect on erectile function is unknown (39). Likewise, there is limited knowledge as to potency in men who have had strokes; presumably, the effect would be dependent on the site and severity of the lesion.

Vascular Disorders

Erection is essentially a hemodynamic phenomenon. Probably the most well-known cause of impotence is Leriche's syndrome, or thrombotic obliteration of the aortic bifurcation with resultant pain and claudication of the hips and thighs and impotence in males (196). Arteriosclerosis also affects the iliac, hypogastric, and pudendal vessels, as well as the small arteries of the corpora cavernosa. Fibrosis, calcification, and obliteration of the small cavernosal vessels occur with aging (298), and early changes can be identified in young men (27).

The role of vasculopathy in diabetic erectile dysfunction is not clear, and some investigators consider this dysfunction primarily neuropathic (90). This assumption may have developed from two suggestions: First, peripheral neuropathy most often occurs in the legs, it is common in diabetic patients, and it was believed that this peripheral neuropathy also would involve the pelvic and genital areas. Second, diabetic patients often have an enlarged bladder capacity, suggesting a relationship between neuropathy and impotence. However, peripheral neuropathy of the legs is rarely associated with disturbances of erection, bowel, or bladder function (287), and up to 30% of bladders with a capacity greater than 800 mL are urodynamically normal (365).

Vascular disease may be an important cause of erectile dysfunction in diabetic patients. As previously discussed, Jevtich and associates (156) found that vascular changes were more common than neurologic changes. More than 95% of the patients had evidence of penile arterial obstruction; 62% of the patients had penile arterial obstruction without any indication of peripheral neuropathy (156). The progressive nature of diabetic vascular changes should be expected to produce a gradual impairment of erectile function. Diabetes also may have an adverse effect on the smooth muscle of the corpora cavernosa. Impaired neurogenic and endothelium-mediated relaxation of penile smooth muscle from diabetic men with impotence has been demonstrated (301).

The “iliac artery steal syndrome” is an unusual manifestation of large-vessel arteriosclerosis (243). Initiation of penile erection occurs normally, but active pelvic movement quickly results in detumescence. It appears that there is collateral circulation in the pelvis to compensate for arteriosclerotic occlusion. During sexual activity, the blood flow is drawn away from the penis to supply the muscles of the hips and buttocks.

Abnormal venous drainage of the corpora also may contribute to the erectile insufficiency. It is well known that creating an artificial venous runoff to treat priapism results in

detumescence, and Ebbehøj and Wagner (85) described spontaneously occurring “venous leaks.” Surgical correction led to erectile improvement. Tudoriu and Bourmer (343) subsequently studied 300 cadaver penises and found evidence that corpora cavernosal leakage is common and that the incidence increases with age. In a study of 49 impotent patients, cavernosography and papaverine-induced erection revealed abnormal venous drainage in 38 patients (206). The term *abnormal venous leakage* is, in the vast majority of

cases, a misnomer. Although some cases of congenitally abnormal venous drainage undoubtedly exist, in most cases, venous leakage is not secondary to venous pathology but is caused by an abnormality of the smooth muscle of the corpora cavernosa. If the corporal smooth muscle does not efficiently relax and allow the cavernous spaces to fill with blood, the subtunical venules are not compressed and blood escapes from the corpora. A more correct term to describe this situation is *corporovenous leakage.*

Endocrine Disorders

In addition to diabetes mellitus, most other major endocrine abnormalities have been associated with impotence. However, the incidence of endocrine disorders in a population of impotent men is not clear. In a prospective study of 256 impotent men, an organic cause was found in 35.9%, a psychogenic cause in 38.3%, and a mixed or uncertain cause in 25.8%. The incidence of hypothalamic-pituitary-gonadal axis abnormalities in the entire group was 17.5%. However, in only 13 of those 45 patients could the impotence be directly related to the axis abnormality (262).

Testosterone is the primary androgen in humans and is secreted by the Leydig cells of the testis in response to LH. The secretion of LH is modulated by LH-releasing factor. These hormones interact in a negative feedback system. Lowering serum testosterone levels causes an increase in LH-releasing hormone, which leads to an elevation of LH. This increase stimulates the Leydig cells to restore the testosterone level to normal. FSH plays an integral role in inducing maximum Leydig cell sensitivity to LH during puberty. After puberty, however, the primary importance of FSH is its action on spermatogenesis.

Low levels of testosterone may result from abnormalities that exist at any point in the hypothalamic-pituitary-gonadal axis. Thus hypogonadism can be characterized as that caused by primary testicular disease or by hypogonadotropic hypogonadism. Testosterone is necessary to maintain male secondary sex characteristics, libido, and probably potency. Thus patients with endocrine abnormalities may present with a variety of symptoms. They may notice a change in body habitus or presence of gynecomastia. Commonly, they note a decrease in the size of the testicles. Physical examination may reveal a diminished size of the prostate and testes. It has been suggested that in adults, testicular size less than 4 cm in length is abnormal (265). A decreased serum total testosterone level confirms the diagnosis of hypogonadism. In cases of alcoholism, massive obesity, or thyroid dysfunction, a serum free testosterone level should be measured because decreased testosterone levels may be the result of low levels of testosterone-binding protein rather than endocrine abnormalities.

If testosterone is low, gonadotropin levels should be measured. Decreased or normal levels of LH and FSH indicate hypogonadotropic hypogonadism, whereas elevated levels of the

gonadotropins in the presence of decreased testosterone levels indicate primary testicular dysfunction.

Hypogonadotropic Hypogonadism

Hypogonadotropic hypogonadism is caused by disorders of the pituitary and hypothalamus and may be part of a clinically recognized syndrome such as Kallmann's syndrome, Prader-Willi syndrome, Laurence-Moon-Biedl syndrome, or cerebellar ataxia (265). Hypogonadotropism may be secondary to a mass lesion or other endocrine disease, such as Cushing's syndrome, acromegaly, panhypopituitarism, hyperthyroidism, or hypothyroidism. Evaluation of hypogonadotropic hypogonadism should include anatomic studies to rule out a mass lesion or brain tumor and a complete endocrine evaluation.

Hypergonadotropic Hypogonadism

Nickel and associates (262) found that 7% of impotent patients had hypergonadotropic hypogonadism or primary testicular failure. Hypergonadotropism can be associated with chromosomal abnormalities, or it can be secondary to infection, surgery, or trauma. In the 18 patients with hypergonadotropic hypogonadism described, 2 had previously undiagnosed Klinefelter's syndrome and 13 had a history of an acquired testicular disorder, small atrophic testicles, and/or a low serum testosterone level. The remaining three patients had psychogenic impotence.

Hyperprolactinemia

Prolactin is secreted by the anterior pituitary under hypothalamic control. Inappropriate elevation of serum prolactin in some patients with pituitary tumors has been associated with galactorrhea and hypogonadism. Hyperprolactinemia also may be secondary to drugs or renal disease. Franks and Nabarro (109) reported impotence as the presenting symptom in 8 of 21 patients with prolactin-secreting pituitary tumors. In male patients with pituitary tumors and normal prolactin levels, only 2 of 19 were impotent. They recommended that “serum prolactin estimations should be made in the course of investigation of all patients with impotence.” Other investigators have challenged this recommendation, and in a careful study of 30 impotent males and 11 potent control subjects, Miller and associates (244) found no significant differences in serum prolactin levels among control, organically impotent, or psychogenically impotent patients. They concluded that impotence is not related to hyperprolactinemia per se and that the routine use of serum prolactin measurements in unscreened patients with impotence should be questioned.

Thyroid Dysfunction

The direct effect of thyroid disease on sexual function is unknown; however, occult hyperthyroidism has been implicated

as a cause of impotence (329). Thyrotoxicosis is associated with increased testosterone levels but normal levels of unbound free testosterone. This is caused by the increased levels of testosterone estrogen–binding globulin associated with hyperthyroidism. Elevated levels of total free estradiol, as well as LH, have been noted (64) and may be associated

with gynecomastia, impaired spermatogenesis, decreased libido, or erectile dysfunction (169). Whether the erectile dysfunction is caused by hormonal abnormalities or what the overall impact of the thyrotoxicosis is are both unknown.

Renal Insufficiency

Chronic renal failure and hemodialysis result in a dramatic decrease in male sexual function (304,341). Even though most impotent uremic men have evidence of peripheral neuropathy, endocrine changes also have been noted and associated with impotence in these patients. Sherman (317) evaluated 14 patients with chronic renal failure receiving hemodialysis with neurologic, psychiatric, and endocrine studies. Seven of the patients were impotent, and all seven had prolonged nerve conduction velocities and absent bulbocavernosus reflexes. However, these patients also had abnormally low serum testosterone levels. Uremia appears to affect Leydig cell function. Guevara and associates (133) noted decreased testosterone levels with increased LH and normal FSH levels in their study of 26 men receiving hemodialysis. Thurm (341) noted that patients with chronic renal failure who were receiving home dialysis maintained a higher level of sexual activity than those receiving hospital-based dialysis. Of 10 patients dialyzed at home, 8 maintained adequate sexual relations. Of 12 patients dialyzed at the hospital, 10 were completely impotent and 2 had little desire for intercourse.

The psychologic and physiologic milieu of patients with chronic renal insufficiency is complex. For instance, the treatment of chronic renal failure associated anemia with recombinant human erythropoietin improves not only the quality of life but also sexual function (263). In addition, many of the drugs used in their treatment, particularly antihypertensives and antidepressants, have been implicated as a cause of erectile dysfunction. After renal transplantation, most patients report a return to preillness levels of sexual activity (304). Successful renal transplantation results in restoration of low serum testosterone levels to normal and improved erectile function in 70% to 80% of patients (304). If impotence persists after transplantation, it is likely related to abnormalities of the blood supply to the penis. Often, the internal iliac artery is used in an end-to-end anastomosis to the transplant renal artery. If a second transplant is performed with the opposite internal iliac artery in a similar fashion, the problem of impotence is markedly increased (127). It is now recommended that second renal transplants be performed with an end-to-side technique on the external iliac or common iliac artery (127).

Traumatic and Surgical Disorders

Trauma to the lower urinary tract reportedly causes impotence in a high percentage of patients. Most patients with a fractured pelvis have multisystem injuries, and there is a high incidence of injury to the bladder and posterior urethra. Up to 50% of these patients may be impotent (125). The initial management of posterior urethral injuries appears to influence potency rates. Patients managed by initial suprapubic cystotomy and later reconstruction have a lower incidence of impotence than those managed by primary repair (70,228).

Many urologic surgical procedures can cause impotence. It is common knowledge that radical prostatectomy for carcinoma of the prostate frequently results in erectile dysfunction, and it has been presumed that damage to pelvic nerves and blood vessels is

the cause. However, some patients retain erectile function after radical prostatectomy. Finkel and Taylor found that of 14 patients who claimed preoperative potency and normal sexual performance, 6 (43%) reported postoperative normal erections and sexual intercourse (101a). Walsh and Donker (357) concluded that impotence results from injury to the autonomic innervation of the corpora cavernosa most commonly during dissection of the prostatic apex and transection of the urethra or during division of the lateral pelvic fascia and lateral pedicle. Modifying the procedure to preserve the cavernosal nerves has reduced the occurrence of impotence, and 1 year after surgery, 86% of patients are potent (358). Others have reported lower rates of preservation of potency following radical prostatectomy. Catalona and Bigg (61) found that 63% of men who underwent bilateral nerve-sparing prostatectomy and 39% who underwent a unilateral nerve-sparing prostatectomy were potent postoperatively, with a minimum of 6 months of follow-up. Patient age, preoperative sexual function, and type of surgery (bilateral versus unilateral nerve sparing) are currently recognized as being important factors in determining postoperative sexual function (279). A modification of total perineal prostatectomy that preserves the periprostatic autonomic nerves has been described (366).

The assumption that radical prostatectomy causes impotence has led many urologists to recommend external beam radiation therapy as an alternative. However, this too has been reported to cause impotence in 40% to 60% of patients (10). Interstitial radiation therapy may be less deleterious. Herr (146) reported that 90% of patients treated with iodine-125 implantation retained potency.

The various types of prostatectomy for benign disease also may result in impotence: simple perineal prostatectomy, 29%; suprapubic prostatectomy, 13%; and transurethral

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resection, 5% (101). The mechanisms responsible for impotence after a simple prostatectomy, particularly a transurethral resection, are not clear. Although an organic cause cannot be totally excluded, a psychogenic cause is more likely. The myth that impotence is inevitable after prostatectomy is widely believed by patients and their spouses.

External sphincterotomy has been reported to cause impotence, but it appears that choice of technique may be an important factor. Kiviat (172) noted that 73% of his patients had some degree of erectile dysfunction after undergoing sphincterotomy at the 3 and 9 o'clock positions. Whitmore and associates (370) reported that of 28 patients who underwent lateral incisions of the external sphincter, 7% had a complete loss of erectile function and 14% had partial loss. They recommended that sphincterotomy be done at the 12 o'clock position and reported that, of 62 patients so treated, none had subsequent erectile dysfunction.

Leriche and Morel (196) first described impotence caused by infrarenal occlusion, and it is now known that approximately 80% of men who present with aortoiliac occlusive disease have significant erectile dysfunction (167). In men with reportedly normal preoperative potency, 21% to 88% have iatrogenic sexual dysfunction after aortoiliac revascularization (76). Ischemia secondary to diversion of pelvic blood flow and/or injury to the autonomic nerves during aortoiliac dissection have been proposed as the causes for postoperative impotence (106). A careful nerve-sparing aortic dissection and attention to preservation of

improvement of pelvic blood flow have been reported to yield much improved results (76,299). Flanigan and colleagues (106) reported 110 men who underwent aortoiliac revascularization and whose sexual function was evaluated preoperatively and postoperatively; 30 patients (27%) were impotent both preoperatively and postoperatively, 67 patients (61%) had normal sexual function preoperatively and postoperatively, and 13 patients (12%) who were impotent preoperatively regained erectile function after surgery. No patient who was potent preoperatively was impotent postoperatively. The actual mechanism by which preservation of preaortic autonomic nerves preserves potency is unclear because it is known that complete preaortic retroperitoneal lymph node dissection with dissection of those nerves may result in ejaculatory incompetence because of absent seminal fluid emission or lack of bladder neck closure but does not cause erectile dysfunction (166,179). Also, the restoration of potency to preoperatively impotent men is most logically caused by reestablishment of pelvic blood flow because autonomic nerve function is unlikely to be enhanced.

The occurrence of erectile dysfunction after surgery for lower bowel disease seems to be dependent on the patient's age and the extent of the surgical resection (364,381). Watts and colleagues (361) noted that of 41 men who underwent rectal excision for ulcerative colitis, 8 were older than 50 years of age and 6 of these were impotent after surgery; of 33 patients younger than 50 years of age, only 1 was impotent postoperatively. Weinstein and Roberts (364) reported 24 men who had undergone colorectal resection (13 abdominoperineal resections and 11 anterior resections). None of the patients who underwent abdominoperineal resection were sexually active after surgery, whereas 8 of the 11 patients having an anterior resection remained sexually active. Two of the three who were not sexually active also had undergone a prostatectomy. The average age of these 24 patients was 64 years. In another review of 45 men undergoing rectal excision, all were younger than 50 years of age. Of 25 undergoing proctocolectomy, 1 (4%) was impotent postoperatively, and of 20 undergoing abdominoperineal resection, 3 (15%) were impotent (381).

Drug-induced Impotence

Medication may be the single most common cause of sexual dysfunction in our society. In a study of 1,180 men screened at one outpatient clinic, 401 were impotent. Of 188 who were more thoroughly evaluated, the most common cause of impotence was medication (324). The adverse effects of medication may be manifest as changes in libido, diminished erectile ability, or decreased ejaculatory capacity. Theoretic mechanisms for these drug effects include production of CNS sedation or depression, drug-related hyperprolactinemia, direct antiandrogen effects, or anticholinergic and antiadrenergic effects (151).

Even though many classes of drugs may affect erectile function, the two most often implicated are antihypertensive and psychiatric or antidepressant compounds. Antihypertensives are categorized as diuretics, vasodilators, or sympatholytics. Most antihypertensives have been associated with some erectile impairment, but diuretics seem to cause relatively few side effects. Thiazides and spironolactone may depress libido, and spironolactone causes enough hormonal alteration to result in gynecomastia (151,269).

Spironolactone's sexual side effects have been attributed to endocrine dysfunction (202).

Despite its innocuous reputation, hydrochlorothiazide may have significant effects on sexual function. It alone was implicated as the cause of impotence in 9% of 861 patients at the Naval Medical Center in Oakland, California (149). The Medical Research Council of Great Britain (236) reported that 36% of patients taking bendrofluazide were impotent. Bulpitt and Dollery (48) questioned 477 patients in a hypertension clinic and found that 31% of men taking diuretics alone complained of impotence.

Sympatholoytic antihypertensives often are associated with impotence. Guanethidine, an agent that blocks peripheral adrenergic nerve activity of postganglionic neurons, is reported to cause impotence. In addition, retrograde ejaculation occurs in nearly two-thirds of patients treated with guanethidine (282). Phenoxybenzamine, an α-adrenergic

blocking agent, may inhibit emission and ejaculation, but erection is apparently unaffected (246). Prazosin, a selective α-adrenergic receptor blocking agent, is believed at present to cause few sexual side effects (379). At high dosages, the β-adrenergic blocking agent propranolol may impair libido and erectile function (269,282). Several studies have reported impotence associated with propranolol, with an incidence as high as 15% (269).

Centrally acting sympatholytic agents include methyldopa, clonidine, and reserpine. With these agents, impotence may be more common and ejaculatory dysfunction less so (234). Because these drugs have a central action, this pattern of dysfunction is not surprising (282). Methyldopa may cause erectile failure in 25% to 33% of patients (346). It causes increased serum levels of prolactin, and it also may cause sedation and depression (151). Twenty-six percent of patients receiving methyldopa have been reported to complain of sexual dysfunction, but these undesirable side effects disappeared within 2 weeks of discontinuing the drug and instituting propranolol and hydralazine (269). The sexual dysfunction associated with clonidine is dose dependent and appears to be caused by the central effects of the drug. Impotence occurs in up to 25% of patients taking clonidine (282), and decreased libido is common (266,269). Reserpine, an agent that may cause significant depression, has been associated with both impotence and failure of ejaculation (282). It remains unclear as to whether erectile dysfunction reported to be secondary to antihypertensive medications is caused by the medication per se or is simply the result of decreasing the systemic blood pressure.

Antidepressant agents, including tricyclic antidepressants and the monoamine oxidase inhibitors, have central and peripheral actions. The tricyclic antidepressants possess sedative and anticholinergic effects and have been associated with decreased libido and impotence. Monoamine oxidase inhibitors interfere with the metabolism of sympathomimetic amines and are reported to cause diminished libido, erectile dysfunction, and impaired ejaculation (233).

Various commonly used drugs have been implicated as being causative factors in erectile dysfunction. Many of the tranquilizers, including the benzodiazepines and meprobamate, have been reported to reduce libido and consequently cause impotence (346). Decreased libido and impotence have been reported to be the most common side effects in patients taking clofibrate, an agent used to treat hyperlipidemia. These symptoms were noted in 14.1% of 1,065 patients taking this drug (269). Cimetidine, a histamine (H_2) receptor agonist used in the treatment of duodenal ulcer disease, has been associated with

diminished libido and impotence in up to 50% of male patients (155). The mechanism by which cimetidine adversely affects male sexual function is unclear. Cimetidine therapy has been associated with gynecomastia and elevated prolactin levels (55,135). Peripheral H_2-receptor blockade in penile corporal smooth muscle also has been suggested as a mechanism (5). Although numerous pharmacologic agents have been implicated in sexual dysfunction (313), few well-controlled studies using objective parameters of sexual function have been performed to evaluate the effects of drugs on libido and penile erection.

Masters and Johnson (227) reported that alcohol was the second most common cause of impotence in their patients. Alcohol has been reported to cause depression of serum testosterone levels in intoxicated male alcoholics and in nonalcoholic men who are given large amounts of alcohol for several days. No similar depression was seen in nonalcoholic males after an episode of acute intoxication (297). Even though increased sexual activity has been attributed to alcohol because of decreased inhibitions, high levels can depress sexual arousal (296) and result in transient impotence. Cannabis, cocaine, and opiates also have been implicated in sexual dysfunction (313).

Psychogenic

All types of male sexual dysfunction, including impotence, premature ejaculation, and ejaculatory incompetence, may have a psychologic origin. Kaplan (159) described the normal sexual response cycle as having two phases: the excitement phase and the orgasmic phase. The excitement phase is characterized by both the subjective (being “turned on”) and objective (erection) changes commonly associated with sexual arousal. The objective manifestations of the excitement phase are dependent primarily on parasympathetic stimulation. The orgasmic phase is postulated to be under both sympathetic and voluntary control.

Men with primary psychogenic impotence often come from sexually repressed or religiously orthodox family backgrounds where sex was not discussed or was treated as sinful and immoral (225). The pathogenesis of secondary psychogenic impotence is poorly understood, possibly because the causes are so varied, and it may be the endproduct of an admixture of temperamental, emotional, familial, affective, cognitive, cultural, maturational, and biologic factors (199). Secondary psychogenic impotence is characteristically rapid in onset and selective in nature, occurring in one set of circumstances but not in others. Performance anxiety is regarded by many as the final common pathway to psychogenic impotence. In the classic example, the initial episode of erectile dysfunction may have a specific and explainable cause, such as intoxication or depression or the fear of discovery in a clandestine encounter. If the man were to approach the next encounter with fear and apprehension, he is likely to fail again, thus entering a vicious cycle of performance anxiety and erectile failure.

Psychogenic impotence can be more narrowly defined as either deficiency of desire (desire inhibition) or inability to maintain excitement even though it is present initially (excitement inhibition) (199). This distinction is important because excitement inhibition, including performance anxiety,

is treated more successfully than desire inhibition. Men with excitement inhibition often

assume the “spectator role” (227) and remain vigilantly preoccupied with their erections and performance. These individuals often can be helped by sex therapy techniques. Most psychologically impotent men suffer from desire inhibition. Desire deficiency has many and varied causes, such as systemic illness, drugs, biologic disorders (e.g., Klinefelter's syndrome), and depression. Psychogenic desire deficiency tends to be situation specific or partner specific. This characteristic helps distinguish it from desire deficiency resulting from other causes.

Evaluation

Much of the interest in male sexual function and dysfunction can be traced to the work of Kinsey and associates (171). Public awareness of scientific advances in this field, particularly the introduction of acceptable and reliable therapy in the 1980s and 1990s, has resulted in increasing numbers of patients being evaluated and treated for impotence. Patients usually desire a quick remedy. The physician must remember that penile erection is a complex phenomenon and that the causes of erectile dysfunction are many, varied, and often interrelated. Education of the patient of this fact at the initial visit is often helpful; the patient needs to understand that organic impotence results in significant psychogenic overlay, just as primary psychogenic problems can result in impotence.

History and Physical Examination

At the initial visit, a careful history and physical examination are mandatory and are the most important part of the overall patient evaluation. The history should focus not only on medical problems that may relate to the patient's impotence but also on the specifics of the sexual dysfunction. Although almost any erectile dysfunction perceived or experienced by a given patient can be loosely defined as impotence, unrealistic patient expectations can be ascertained relatively easily. The duration and nature of onset of impotence often aid in differentiating a psychogenic from an organic cause. Patients with psychogenic impotence usually experience a rather abrupt onset of symptoms. Not uncommonly, this is associated with a traumatic event, such as a family death, job loss, or birth of a child with a congenital deformity. To the contrary, most causes of organic impotence result in a slow but progressive deterioration in erectile capacity. Changes in libido should be ascertained and, if present, may signify hormonal abnormality. The presence of morning erections and the occurrence of erections in situations apart from the usual sexual partner are important historical clues. A history relating to risk factors previously discussed should be obtained. Symptoms compatible with intermittent claudication should be sought. Specific questions related to systemic disease (e.g., atherosclerosis, diabetes), previous pelvic surgery, radiation therapy, bowel or bladder symptoms (indicative of neurologic disease), and cryptorchidism should be asked. The medications the patient is taking should be noted. As previously discussed, various drugs, but particularly those that act on the nervous or vascular systems, have been associated with erectile dysfunction. All unnecessary medications should be discontinued. Although it is reasonable to attempt to change dosages or medication in patients who require pharmacologic therapy for hypertension or psychiatric disease, such efforts in our experience generally have not proved to be beneficial.

A physical examination should be performed with particular attention to identifying vascular, neurologic, hormonal, and genital abnormalities. The femoral and peripheral pulses should be palpated and the abdomen and femoral areas auscultated for bruits. A limited neurologic examination should be performed. Perineal sensation in the area of the sacral dermatomes to pinprick, as well as the quality of rectal tone, should be ascertained. The presence or absence of a bulbocavernosus reflex, elicited by simultaneously squeezing the glans penis and noting anal sphincter activity, should be noted. A rectal examination to evaluate the prostate gland and palpation of the penis to identify plaques suggesting Peyronie's disease should be performed. The size, position, and consistency of the testes should be noted. The physical examination also should include an assessment of the character and distribution of body and facial hair, as well as gynecomastia, which may indicate a hormonal abnormality.

Additional Evaluation

There is little agreement concerning the optimal evaluation of the impotent patient after the initial history and physical examination. We initially obtain a serum testosterone measurement and serum multiple analyses in addition to urinalysis. Serum prolactin is not routinely measured, but the level is determined when an abnormally low serum testosterone level is found or when a history of decreased libido is obtained. The need for any “routine” endocrine testing has been questioned. Performing hormonal screening on only those patients with clinical signs of hypogonadism, that is either decreased libido or bilateral testicular atrophy, has been advocated (157). Thyroid function tests are performed only if there is suspicion of thyroid disease from history or physical examination. We do not perform routine psychometric testing. In patients with low morning levels of testosterone, serum levels of prolactin, LH, and FSH are determined.

The evaluation of most patients can reasonably stop after the history, physical examination, and blood studies just discussed are complete. We do not routinely perform vascular studies. Therefore patients older than 50 years of age with significant vascular risk factors, such as previous myocardial

infarcts, cerebrovascular accidents, hypertension, diabetes, or a strong family history of vascular disease, generally are not studied (129). Since the advent of successful medical therapy for erectile dysfunction, one can argue that initial vascular studies are rarely indicated. Neurologic testing, including measurement of sacral reflex latency time, is performed only in patients with suspected neurologic lesions and is rarely indicated or clinically useful. Urodynamic evaluation also may substantiate a suspected neurogenic component. Urodynamic evaluation also helps identify a patient requiring cystoscopy or transurethral resection of the prostate before the placement of a penile prosthesis. Finally, we do not routinely perform nocturnal penile tumescence testing.

The evaluation of patients presenting with impotence is not standardized and is controversial. Many of the methods currently used have been criticized because of the lack of standardization and normal control data.

Vascular Studies

For years, the most commonly used method for evaluating penile arterial blood flow was calculation of the penile-brachial index (PBI). These measurements are obtained with a 10-mHz Doppler probe positioned over the penile arteries. A pneumatic cuff is placed around the base of the penis and inflated until arterial flow ceases. The cuff is slowly deflated, and the point at which arterial flow is reestablished is the penile systolic blood pressure. The penile systolic blood pressure divided by the brachial systolic blood pressure yields the PBI. In general, a PBI of less than 0.60 is thought to be indicative of vasculogenic impotence (124). Most clinicians and investigators have abandoned the evaluation of the penile arterial supply with Doppler measured blood pressure indexes for several reasons. The Doppler signal is not specific, and the exact vessel being studied is difficult to ascertain. In addition, determinations are made with the penis in the flaccid state, and the findings may not be applicable to the erect penis. Finally, the study is operator dependent. Because of these shortcomings, measurement of the PBI has been largely abandoned.

Penile angiography should be reserved for patients who are potential candidates for a revascularization procedure. Suitable surgical patients are those with a demonstrable and surgically correctable arterial occlusion and patent distal flow. Even though a high proportion of organic impotence is vasculogenic, a relatively small proportion of patients are good candidates for angiography and revascularization (126,232).

Arteriography usually involves selective bilateral internal iliac visualization or selective pudendal arteriography. Some investigators recommend that the procedure be formed with the patient under general anesthesia. McDougal and Jeffrey (232) have found that these highly motivated patients often can be studied when liberal doses of intravenous diazepam and morphine are administered. Other investigators have stated that in unanesthetized patients, approximately 50% of apparent obstructions of the penile artery or its branches are functional in origin (40). In addition, visualization of penile arteries can be enhanced by the use of vasodilators injected either intraarterially or intracorporally.

Nocturnal Penile Tumescence

Erections during sleep were reported as early as 1940, but it was not until 1953 that Serinsky discovered rapid eye movement (REM) sleep and noted that the cycles of nocturnal penile tumescence (NPT) closely resembled the cycles of REM sleep (163). Subsequently, Fisher and associates (104) reported that in young males, nocturnal erections were definitely related to REM sleep and occurred five or more times nightly. Karacan and associates (163) found that NPT associated with REM sleep was most common in pubertal males and showed a steady decline in frequency and duration with aging. They also noted that the proportion of NPT associated with non-REM sleep increases with age. These early discoveries led to the development of transducers and recorders used to detect and measure engorgement of the penis, thus providing a reproducible and convenient means to measure NPT.

Karacan and associates (161) soon suggested that in impotent men, the presence of full, sustained erections during sleep was indicative of psychogenic impotence, and the absence of turgid nocturnal erections indicated organic impotence. NPT monitoring quickly became accepted as the only objective means to differentiate psychogenic and organic impotence and was routinely incorporated into the evaluation of erectile dysfunction at many centers.

Some centers use elaborate sleep laboratories and monitor electroencephalographic activity and NPT activity and use video monitoring of erections. Other centers use simpler electronic measuring strain-gauge devices for in-hospital or at-home evaluation. The patient's time and financial considerations in performing NPT testing in a sleep laboratory are obvious.

Some limitations of NPT monitoring became apparent and included both technical problems with the strain gauges and monitors, as well as questions about the basic assumptions of NPT testing. The premise of NPT testing rested on the belief that normal penile tumescence detected by an average increase in circumference of 30 mm (15 to 45 mm) indicated that a rigid erection had occurred. Wein and associates (363) noted that 23 of 134 patients tested for nocturnal erections had significant penile expansion but did not achieve rigidity adequate for vaginal penetration. It became clear therefore that rigidity as well as expansion was an important parameter of penile erection.

To assess rigidity, the penile buckling pressure has been measured. When an erection is present, a pressure device is pressed against the glans penis and the pressure required to make the penis buckle is measured in millimeters of mercury. If the penis buckles at a pressure of less than 60 mm

Hg, it is too soft for vaginal penetration. If the penis does not buckle at pressures of 100 mm Hg or more, it is rigid enough for intromission. Buckling pressures between 60 and 100 mm Hg are equivocal (162).

Part of the controversy surrounding NPT stems from uncertainty as to the validity of NPT testing. The basic presumption is that the absence of nocturnal erections indicates organic dysfunction. This premise is not universally accepted. A number of investigators have noted that dreams with high anxiety content may not be associated with NPT at all (160) or may cause rapid detumescence (104). Conversely, there are numerous cases of patients with abnormal NPT patterns suggestive of impotence who report normal coital activity (314). On the basis of NPT testing, certain organic conditions may be misdiagnosed as psychogenic. Patients with hyperprolactinemia or “pelvic steal syndrome” are in this category (314). NPT testing alone is not adequate to differentiate psychogenic from organic erectile dysfunction. The presence of rigid nocturnal erections strongly supports a diagnosis of psychogenic impotence. The significance of impaired or absent nocturnal erections is not known, and in some instances, men with psychogenic impotence may not have nocturnal penile tumescence. Because of these shortcomings, NPT testing is not indicated for routine use (257).

Intracorporal Injection, Cavernosography, and Cavernosometry

The hemodynamic changes associated with penile erection involve increased arterial inflow, sinusoidal relaxation, and decreased venous outflow. Histologic studies show that smooth muscle is present in the walls of the sinusoids, as well as the walls of the penile arteries (205,208). In 1982, Virag (352) reported the discovery that intracorporal injection of the vasodilating drug papaverine resulted in penile erection. Subsequently, other drugs, such as phenoxybenzamine, and drug combinations, such as papaverine and phentolamine, have shown similar effects (42,385). Multiple other agents injected intracorporally, such as

imipramine and verapamil, also have been reported to produce erection (43). PGE_1 alone or in combination with other agents (papaverine and phentolamine) is currently the most widely used drug for intracorporal injection (24,331). Maximum erection is usually evident within 10 to 20 minutes. Having the patient stand or kneel has been reported to enhance penile engorgement, and some patients require sexual stimulation to achieve maximum rigidity (385). Erection, or at least engorgement, lasts from a few minutes to several hours but in some cases may last much longer. Priapism is a significant complication associated with intracorporal injection and is discussed later.

The production of an erection with the intracavernosal injection of vasoactive drugs allows the penis to be evaluated in the erect state. In fact, the production of a rigid erection following intracavernosal injection has been interpreted to indicate that the penile vasculature (both arterial inflow and corporovenous occlusion) was intact. However, some evidence indicates that the production of an erection by this technique does imply normal corporovenous occlusive function but not necessarily normal arterial inflow. In 19% of cases with a rigid erection following intracavernosal injection, evidence of arterial occlusive disease existed (272).

Like low arterial inflow, abnormal or excessive corporovenous “leakage” from the penis causes impotence. Venous deterioration with increased leakage has been implicated as a cause of impotence in older men (343). The use of cavernosography and saline infusion techniques to determine venous outflow has been reported by a number of investigators (260,351,368). In these studies, however, there was no vasodilation or sinusoidal relaxation such as that pharmacologically induced by papaverine injection. Lue and associates (206) reported their findings with cavernosography during papaverine-induced erection. Because patients with arterial insufficiency would not benefit from cavernosography, they eventually selected patients who were unable to achieve or maintain a good erection but who had an excellent arterial response to papaverine as shown by pulsed Doppler analysis and sonography. In their study of 49 patients, 38 had evidence of abnormal venous drainage. They noted that an intracorporal pressure of 80 mm Hg almost completely stops venous outflow. If intracorporal pressure does not reach 80 mm Hg after papaverine injection, saline solution should be infused to produce further venous occlusion. Normal emissary veins should be occluded at this pressure, and only abnormally large veins remain open. If further infusion of 100 mL of saline at 80 mL per minute cannot increase the intracorporal pressure to 80 mm Hg, a large venous leak is diagnosed and can be localized with contrast cavernosography (206). The patients with excellent arterial dilation and blood flow after papaverine injection are the ones who are reported to benefit most from erection cavernosometry and cavernosography and are thought to be the most suitable candidates for venous ligation procedures.

The method used to diagnose venous leakage by cavernosometry and cavernosography is not standardized. It appears that cavernosometry after the intracavernous injection of vasoactive drugs provides more valuable information than cavernosometry performed with saline infusion alone (337). The best drug to use, optimal dosage, and best criteria to use to diagnose venous “leakage” are still unclear. The Society for the Study of Impotence has determined that a significant corporovenous leak should be diagnosed by either maintenance flow rate or by dynamic infusion cavernosometry and cavernosography (129).

If the maintenance flow rate 10 minutes after 45 to 60 mg of papaverine or 10 µmg of PGE_1 injected intracorporally is greater than 30 mL per minute to maintain intracavernous pressure greater than 90 mm Hg or to produce a fully rigid erection, abnormal venous leakage is diagnosed (31). The clinical effectiveness of cavernosometry

and cavernosography is limited by several factors, including lack of normative data, operator dependence, variable interpretation of results, and poor predictability of the therapeutic outcome of venous surgery.

Neurologic Testing

When the history or physical examination indicates a potential neurologic cause for impotence, neurologic testing can be performed, although it is rarely clinically useful. Two important points need to be remembered. First, the presence of a demonstrable neurologic lesion does not mean that the lesion is responsible for the erectile dysfunction. Second, the neurologic studies used do not directly measure the integrity of the autonomic nerves that control penile erection.

The integrity of neural pathways can be ascertained by measuring evoked potentials. Both sacral-evoked potentials and genitocerebral-evoked potentials can be used (134,184). These studies require sophisticated instrumentation and have significant limitations in the evaluation of impotence. The sacral-evoked potential (sacral latency) is essentially an electrophysiologic procedure that measures the bulbocavernosus reflex (184). When this test is performed, the penile skin is stimulated and recordings are made from a needle electrode placed in the bulbocavernosus muscle. The time from stimulation to the first response in the bulbocavernosus muscle (latency) is measured.

Penile erection is normally governed by a reflex arc consisting of pudendal afferent (sensory) fibers and parasympathetic efferent (motor) fibers. The sensory portion of the reflex that governs erection and the sensory portion of the reflex, which is measured by sacral-evoked potential studies, are therefore identical. This portion of the reflex arc also can be evaluated by performing dorsal penile nerve conduction velocity (122). At present, however, the efferent (parasympathetic) portion of the reflex controlling erection cannot be accurately evaluated. The sacral-evoked response measures reflex activity over pudendal sensory nerves and pudendal (somatic) motor nerves. This study provides information concerning some reflex activity through the sacral spinal cord, but it does not directly test penile innervation.

Similar problems are faced by urologists in attempting to ascertain whether the motor fibers to the urinary bladder are intact. A cystometrogram that demonstrates detrusor contractions indicates that the parasympathetic motor fibers to the bladder are intact. When no detrusor activity is elicited, however, one cannot conclude that the bladder is denervated. Cystometry has been used as a study of the parasympathetic motor fibers in impotent patients, but its usefulness is limited. Impotent patients with obvious neurologic disease and voiding symptoms often have abnormal cystometrograms, but this study adds little useful information to the overall evaluation. Cystometry is rarely helpful in patients with no significant neurologic or urologic disease and a normal neurologic examination.

The objective measurement of the status of the CNS as it relates to erectile dysfunction is even more limited. Genitocerebral-evoked responses can be measured. The penis is stimulated as in the sacral-evoked response study and recordings made from electroencephalographic leads on the scalp (134). As with other neurologic studies, an abnormal genitocerebral-evoked response must be interpreted with caution. Although a neurologic abnormality may be demonstrated, it may bear no relationship to the patient's complaint of impotence. Neurologic tests are rarely indicated in the evaluation of the patient with erectile dysfunction. No available neurologic study can determine whether penile innervation is intact, and neurologic testing adds little to information gained from the history and physical examination.

Management

Drug Therapy

Oral Drug Therapy

Yohimbine, an indolic alkaloid obtained from the yohimbine tree, currently is used in the treatment of erectile dysfunction. For many years, this drug has been considered an aphrodisiac. This agent, in combination with testosterone and nux vomica extract, was in widespread use for the treatment of impotence in the 1960s (224,245,328). Morales and colleagues (251) reported that 6 of 23 patients given this drug "reported the reappearance of full and sustained erections and resumption of satisfactory sexual performance." A subsequent report (250) showed no statistical difference between yohimbine and placebo in treating patients with organic impotence. A well-known side effect of the antidepressant drug trazodone is priapism. For this reason, this antiserotoninergic drug has been advocated for the treatment of erectile dysfunction, particularly psychogenic impotence. Little data on this drug's efficacy exist, but preliminary data suggest that response to trazodone is significantly better than that to placebo (188).

A significant advance in the medical therapy of erectile dysfunction occurred with the U.S. Food and Drug Administration approval of sildenafil (Viagra) in 1998. This selective type-5 phosphodiesterase (PDE) inhibitor is approximately 4,000 times more selective for type-5 PDE than for type-3 PDE and 10 times more selective for type-5 PDE than for type-6 PDE (12). Nitric oxide released from nerves or endothelium causes an increase in cGMP, which results in smooth muscle relaxation. Type-5 PDE causes the breakdown of cGMP in corporal smooth muscle. The inhibition of type-5 PDE results in accumulation of cGMP and promotes cavernosal smooth muscle relaxation (335). *In vivo,* sildenafil increases intracavernosal pressure in response to cavernous nerve stimulation (57). The direct injection of sildenafil into the penis, however, does not produce a rise in intracavernous pressure (8). In addition, administration of

sildenafil to animals that have undergone bilateral cavernous nerve transection and have been exposed to erectogenic central stimuli fails to increase intracavernous pressure (8). These data support the concept that an intact neural input is necessary for sildenafil to be effective.

Sildenafil has been reported to improve erections in patients with psychogenic, organic, and mixed factors. Many trials have shown that the success rate of sildenafil use is in the range of 65% to 80% (335). In a meta-analysis of data from 3,361 patients with predominately organic erectile dysfunction, sildenafil improved erections to a degree sufficient for intercourse always or almost always in 48% of patients with severe erectile dysfunction, defined as the inability to ever obtain or maintain an erection (334). Men with destruction of both cavernosal nerves would be unlikely to respond to sildenafil. Following radical prostatectomy, the efficacy of sildenafil appears to be greatest in men who have undergone bilateral nerve-sparing surgery, less with unilateral nerve-sparing surgery, and least with ablation of both cavernosal nerves (384). Because many patients with erectile dysfunction, regardless of etiology or prior therapy, can potentially respond to sildenafil, this drug can be recommended as first-line therapy in the absence of a contraindication to its use.

An absolute contraindication to the use of sildenafil is the concomitant use of nitrates. The use of these two drugs in combination can lead to a precipitous drop in blood pressure. The use of sildenafil in patients with cardiovascular disease is controversial (62). Side effects with sildenafil use include nasal congestion, dyspepsia, and diarrhea. In addition, approximately 3% of men taking sildenafil experience blurred vision or a visual color tinge. These visual disturbances have been attributed to the fact that sildenafil is only ten times more selective for type-5 than for type-6 PDE, which is present in the retina.

Testosterone Therapy

The alkylated testosterone drugs methyltestosterone and fluoxymesterone have been widely used primarily because they can be given orally. Both agents have the significant disadvantage of poor gastrointestinal absorption and liver toxicity (375). For these reasons, their use has been replaced by the parenteral use of intramuscular esterified testosterone. The National Institutes of Health (NIH) Consensus Development Conference Statement on impotence (257) recommended that “oral androgens, as currently available, are not indicated.” Significant side effects can occur with testosterone therapy. Despite the fact that hepatotoxicity has been markedly reduced when esterified rather than alkylated testosterone is used, evaluation of liver function studies before and periodically during therapy is prudent. No evidence exists implicating testosterone therapy as a cause of prostate cancer, but testosterone is contraindicated in the presence of prostate cancer. Patients receiving testosterone should be monitored with digital rectal examination and serum prostate-specific antigen determination. Androgen therapy also has been demonstrated to increase hematocrit and red blood cell volume by stimulating erythropoietin production. Patients with hematocrit values greater than 48% appear to be at risk from cardiovascular complications (187).

Intracorporal Injection Therapy

The use of intracorporal injection of vasoactive agents has been described previously. Initial clinical trials using intracorporal papaverine and combinations of papaverine and phentolamine in the treatment of impotence reported excellent results, particularly in the therapy of impotence secondary to neurologic causes (320,385). PGE_1 has been advocated

as being superior to either papaverine or combinations of papaverine and phentolamine. PGE_1, like papaverine and phentolamine, causes relaxation of corporal tissue *in vitro* (140). In addition, enzymes that locally metabolize PGE_1 are present in penile tissue, and therefore the risk of priapism is at least theoretically reduced (294). Large clinical series have been reported, which attest to not only the efficacy but also the low complication rate (including priapism) with the use of this agent (153,331). The use of a drug combination of PGE_1, papaverine, and phentolamine also has been advocated (24).

Significant complications of the use of intracorporal papaverine alone, combinations of papaverine and phentolamine, and PGE_1 have occurred. The development of fibrotic penile lesions has been reported (69), and penile nodules have been reported to occur in up to 57% of patients who administer their own injections for 1 year (198). The acidic pH of papaverine may be related to the development of these fibrotic lesions. In animal studies, long-term use of intracorporal papaverine causes not only fibrosis in the area of the injection sites but also smooth muscle hypertrophy in other areas of the corpora (3). Hepatotoxicity is a known side effect of papaverine, but this has been an uncommon adverse effect of intracorporal papaverine use (198).

The most significant complication of intracorporal injection therapy for impotence is the development of priapism (136). The true incidence is unknown, but the number of patients who experience priapism is undoubtedly related to the patient population being treated and the type and dose of drug or drug combination being used. In large series, priapism has been reported to occur in less than 1% to 4% of patients (198,321).

The mainstay of therapy of drug-induced priapism has been the intracorporal injection of α-adrenergic agonists. Because erection has been induced artificially by drugs that relax corporal smooth muscle, the injection of agents (α-adrenergic agonists) that contract corporal smooth muscle is both theoretically sound and clinically efficacious (210). Several agents have been recommended, including epinephrine, norepinephrine, metaraminol, and phenylephrine (207,359).

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Phenylephrine appears to be particularly efficacious and results in fewer cardiovascular side effects than the other agents and has become the drug of choice to treat priapism (81). When treating priapism, the recommended dose of phenylephrine is 0.05 mg injected intracavernosally on each side (total dose of 0.1 mg) (359). The use of α-adrenergic agonists has been advocated for initial therapy of priapism of a variety of causes (207). Complications from the treatment of priapism with α-adrenergic agonists have occurred (207,211). Because of the potential for significant cardiovascular morbidity, these agents should be used with care.

Although intracorporal injection therapy is efficacious in a large number of impotent patients, both the patients best suited for this form of therapy and the best drug (and dosage) remain in doubt. For example, patients with neurogenic impotence tend to respond to lower dosages of vasoactive drug than patients with impotence secondary to other causes (321). Only approximately 40% to 50% of patients enrolled in at-home drug injection programs are still administering their own injections after 1 year (198).

Intraurethral Drug Therapy

The intraurethral administration of alprostadil through a novel delivery system designed to administer a pellet of PGE_1 was introduced in 1997. The drug is transferred through the urethral mucosa and corpus spongiosum to the corpora cavernosa. Alprostadil causes activation of adenylate cyclase, which leads to increased levels of cAMP and smooth muscle relaxation. After one pass through the pulmonary vasculature, between 60% and 90% of systemic PGE_1 is inactivated (292). The drug is available in 125-, 250-, 500-, and 1,000-µmg strengths to allow dosage titration. In the initial trials, symptomatic hypotension occurred in 3% of patients, dizziness occurred in 4% of patients, and syncope occurred in 0.4% of patients during in-clinic dosing. For this reason, titration should be carried out under medical supervision. The most common side effect is penile pain, which occurs in 36% of patients. Initial studies indicated that intercourse and erections sufficient for intercourse rates to be approximately 50% to 65% (142,268). Subsequent reports have indicated lower success rates (367).

Vacuum-constriction Devices

Vacuum-constriction devices provide effective and acceptable therapy for erectile dysfunction for some patients. The devices consist of a plastic cylinder, tubing connected to a handheld vacuum pump, and elastic constriction bands (Fig. 42.10). High patient acceptance and low morbidity have been reported (255,377). A survey of 1,517 users of the device revealed that 92% achieved erection with the device, and 77% had intercourse at least every 2 weeks (377). The successful use of this device in difficult clinical settings, such as with patients who have had penile prostheses removed, also has been reported (253).

FIGURE 42.10. Vacuum-constriction device.

Penile Revascularization and Venous Ligation Procedures

Penile revascularization to treat vasculogenic impotence was introduced by Michal. The Michal I operation involved the direct anastomosis of the inferior epigastric artery to the corpus cavernosum. The procedure was abandoned because of many failures within the first months, and the initial success rates of 60% to 70% were modified to 40% when patients were followed for 1 year (316). The Michal II modification involved the anastomosis of the inferior epigastric artery to the dorsal artery of the penis. In their initial series, 13 of 18 patients improved (242). Others have reported similar encouraging results. Of eight patients revascularized by McDougal and Jeffrey (232), four reported normal sexual function, and two reported markedly improved sexual function at least 1 year after the operation. The Michal II operation presumes that blood from the inferior epigastric artery flows into the dorsal artery of the penis and then retrograde to the pudendal artery where it bifurcates into the dorsal and profunda penile arteries. The ideal candidate for this operation is the patient in whom the arterial occlusion is located proximal to the bifurcation

of the pudendal artery into the dorsal and deep penile arteries with patent vessels distally. A modification of the Michal II procedure has resulted in the restoration of coitus with improved erection in 80% of patients (129). Direct revascularization of the profunda penile arteries with the inferior epigastric artery also has been reported (216,261). Venous

arterialization procedures as described by Virag also have been reported to be successful in a significant number of cases (25). These procedures consist of anastomosing the inferior epigastric artery to the deep dorsal vein of the penis with or without the creation of a fistula between the vein and the cavernous body.

Only a limited number of men with vasculogenic impotence are candidates for revascularization procedures. McDougal and Jeffrey (232) have outlined a careful evaluation to properly select patients. Of 44 patients thought to have organic impotence, 28 were found, by venous occlusion plethysmography, to have a penile blood flow measurement of less than 2 $ml^3/100\ cm^3$ of tissue per minute. These 28 patients underwent pudendal angiography, which demonstrated significant arterial occlusive disease in 13, and 11 of those 13 underwent revascularization. In those patients in whom the penile arteries were demonstrated angiographically, the results of revascularization were successful. Angiographic visualization of the penile arteries indicates patency, and the use of tolazoline hydrochloride or another vasodilator may be necessary to avoid false-negative results. The key to successful penile revascularization appears to be careful patient selection.

After the demonstration that increased venous resistance is important in the physiology of normal erection, many investigators have sought the optimal surgical approach for patients with erectile dysfunction secondary to “venous leakage.” Venous ligation surgery was described in the early 1900s by Wooten (380). More recently, Ebbehøj and Wagner (85) reported successful restoration of potency after closure of a venous leak between the corpora cavernosa and the glans. Wespes and Schulman (369) reported an 80% success rate in patients with venous leakage by ligating the deep dorsal vein and its tributaries. Lue (213) has advocated including ligation of the cavernous and crural veins. The rationale for venous ligation surgery in most patients is questionable. Demonstrated “venous leaks” are almost always the result of inadequate relaxation of the corporal smooth muscle and are not primarily a “venous disease.” As reported success rates have fallen, enthusiasm for venous ligation surgery has waned (293). According to the 1993 NIH Consensus Statement on Impotence, “this has tempered enthusiasm for these procedures, which are probably therefore best done in an investigational setting in medical centers by surgeons experienced in these procedures and their evaluation.”

Penile Prostheses

Semirigid Prostheses

The concept of inserting a rigid rod inside the penis to facilitate coitus was a logical extension of the fact that various mammals (e.g., dogs, bears, raccoons, walruses) have a bone-os penis-in the penis. Loeffler and Sayegh (201) reported the first use of an artificial synthetic implant for the correction of organic impotence. They noted that reconstructive

surgeons previously had favored autogenous grafts, but bone usually undergoes absorption when used as a free graft unless placed in contact with living bone. Autogenous cartilage often curled. These two characteristics made the use of autogenous grafts unsuitable in the penis. These investigators constructed a perforated penile implant from acrylic and surgically placed it in the groove between the corpora cavernosa. Absorbable sutures placed through the perforations held it in place until fibrous tissue formation fixed it in position permanently. They later modified these prostheses with silicone for construction (191,192,200,201).

In 1967, Pearman (270) described a silicone prosthesis developed from a mold formed by injecting hot paraffin in the space between Buck's fascia and the tunica albuginea of a cadaver's penis. The resulting prosthesis was a three-fifths circle on cross section and could extend from the corona to the suspensory ligament. Interestingly, one modification of the prosthesis included a metal spring, suggestive of the silicone–silver wire prosthesis introduced by Jonas and Jacobi (158) some years later.

Because of their placement between Buck's fascia and the tunica albuginea, these early implants were prone to instability, displacement, and even extrusion (256). Beheri (22) first suggested placement of prostheses within the corpora cavernosa in 1966. In 700 patients, he implanted paired polyethylene prostheses within the corpora and reported good stability and cosmesis (22). Lash (192) also eventually advocated intracorporal placement, with the prosthesis extending from midglans to pubis. Morales and associates (252) also used intracorporal placement, but the rigidity and narrow contour of the prosthesis caused problems with pain and perforation. Eventually, Small and associates (325) developed paired penile implants with an exterior of medical-grade silicone and a core of silicone sponge (called the *Small-Carrion prothesis*). The prosthesis provided adequate length and, more important, normal width to the penis. Even though firm, it had enough flexibility to keep the phallus inconspicuous while in the normal position or against the abdominal wall. The Small-Carrion prosthesis was introduced in 1975 and was widely used (164,239,240,258,326).

In 1977, Finney (102) introduced a hinged silicone penile implant. He noted that with the Small-Carrion prosthesis, it was not possible to preoperatively determine the appropriate sizing, thus requiring that several sizes be kept available. Also, the implant maintained the penis in an upright, erect state, sometimes requiring constrictive clothing to conceal it. Finney recognized that even though the earlier Lash prosthesis extended only to the pubis and allowed the penis to hang normally, it imparted adequate rigidity to the penile shaft. With these considerations in

mind, he developed a prosthesis with a tail that could be trimmed to facilitate intraoperative sizing, a hinge section at the level of the penis to allow dependent positioning, a rigid shaft, and an anatomically correct conical tip to improve positioning under the glans.

Operative Techniques.

The intracorporal prostheses introduced by Beheri (22) and Morales and associates (252) were inserted through a dorsal midline penile incision. To minimize trauma and scarring to the phallus, Small and associates (325) advocated a perineal surgical approach (Fig.

42.11). The patient was placed in a semilithotomy position and a Foley urethral catheter inserted to help identify the urethra during the procedure. A midline perineal incision was developed from the base of the scrotum toward the anus. Sharp dissection allowed identification of the bulbocavernosus muscle. The bulbocavernosus muscle and urethra were retracted to one side and the ischiocavernosus muscle and penile crus identified. Once identified, the crus was opened longitudinally with a 2- to 3-cm incision. The intracorporal space was developed with Hegar dilators proximal to the ischial tuberosity and distal to the end of the corpus cavernosum. Dilation was performed initially with a no. 5 Hegar dilator and advanced to a no. 10 or 11. The prosthesis of appropriate size was then inserted. The procedure was repeated on the opposite crus. Small and colleagues (325) noted that the 13.3-cm (medium) or the 14.5-cm (long) prosthesis was usually required, and they attempted to use the widest possible prosthesis. The wounds were closed with 3-0 chromic catgut; no drains were left. The Foley catheter was removed immediately after surgery, and broad-spectrum antibiotics were given postoperatively. For patients who were impotent after pelvic fracture or who had a perineal urethroplasty, Small and associates (325) suggested either making the skin incisions laterally directly over each crus or in the midline at the penoscrotal junction, thus avoiding scarred tissue.

FIGURE 42.11. Perineal approach for placement of semirigid penile prostheses: through a midline perineal incision **(A);** the corpus spongiosum and penile crura are exposed and the crus incised **(B).** The corpus cavernosum is dilated distally **(C)** and proximally **(D).** A prosthesis is placed in each corpus cavernosum **(E).** (Redrawn from Small MD, Carrion HM, Gordon JA. Small-Carrion penile prosthesis: new implant for management of importance. *Urology* 1975;5:479.)

The penoscrotal approach was later popularized by Barry and Seifert (18) (Fig. 42.12). They emphasized that even in patients without trauma or previous surgery, there were inconveniences with the perineal approach, such as perineal fat incision and incision of the ischiocavernosus muscles. Damage to the dorsal neurovascular bundle was a possible complication of the dorsal penile approach.

FIGURE 42.12. Penoscrotal approach for the insertion of paired semirigid penile prostheses: through a midline incision the corpus spongiosum (urethra) and corpus cavernosa are exposed **(A);** with traction sutures in the tunica albuginea the corpus cavernosum is incised longitudinally **(B);** the cavernosal space is dilated with the prosthesis or with dilators **(C);** and a prosthesis is placed in each corpus cavernosum **(D).** (Redrawn from Barry JM, Seifert A. Penoscrotal approach for placement of paired penile implants for impotence. *J Urol* 1979;122:325.)

The surgery was performed with the patient in the supine position. A Foley catheter was inserted. A 5-cm midline incision was made over the urethra at the penoscrotal junction. The tissues overlying the urethra were incised to

the level of the corpus spongiosum, then dissected laterally to identify the tunica albuginea. The skin, subcutaneous tissue, and Buck's fascia were retracted laterally and stay sutures fixed in the tunica albuginea. A 5-cm longitudinal incision was made between

the stay sutures. The corpus cavernosum was dilated with Hegar dilators. The procedure was repeated on the opposite side. The prosthesis was inserted, and the incisions in the tunica albuginea were closed with a running 3-0 polyglycolic acid suture. The subcutaneous tissues and skin were closed with 4-0 chromic catgut. During the procedure, a 1-g/dL neomycin sulfate solution was used as wound irrigant. An aminoglycoside or cephalosporin was used preoperatively, and the Foley catheter was removed 24 hours after the procedure (18).

In their introduction of the silicone–silver wire prosthesis, Jonas and Jacobi (158) described a dorsal subcoronal approach. This approach also has been used satisfactorily by others (29). A semicircular dorsal incision is made in the coronal sulcus. Buck's fascia is incised, and a 1- to 5-cm linear incision is made bilaterally in the tunica albuginea. The corpora cavernosa are then dilated with Hegar dilators, and the appropriate length of the prosthesis is determined with the sizer. The prostheses are then inserted, and placement in the distal corpora may be facilitated by the use of an eyelid retractor. The incisions in the tunica albuginea may be closed with absorbable or nonabsorbable suture. Most surgeons recommend the use of preoperative antibiotics, and some advocate use of a mild-pressure dressing (29,158,183). With all of the semirigid prostheses, an implant is placed in each corpus cavernosum. Gaur (117) has advocated in the placement of only one implant, claiming that results were satisfactory and significant cost savings could be realized.

Complications.

Complications associated with the semirigid penile implants are usually related to pain, inappropriate size, or infection. Other serious problems include urethral or skin erosion, urinary retention, or skin necrosis secondary to pressure dressings.

Kaufman and associates (164) reviewed their experience with 1,207 cases, finding that major complications occurred in 7.8%. Before the introduction of antibiotics, the reported incidence of infection was 15%; however, this was reduced to less than 5% with the use of antibiotic protocols (306). Predictably, diabetic patients seem to be at highest risk for developing infection (164,182,306). Before surgery, care must be taken to find any possible source of infection, such as pustules, infected wounds, or infected urine. If such a source is found, surgery must be postponed until the infection has healed adequately. The patient should be shaved at the time of surgery, not the evening before, and should undergo careful preoperative skin preparation with an antiseptic soap. Systemic antibiotics are used routinely. Once an intracorporal infection is established, both prostheses should be removed; the two corpora cavernosa communicate freely, and it is unlikely that an infection will be isolated to one side. Pain lasting longer than 4 weeks is another major problem. It appears that diabetic patients are more likely than nondiabetic patients to have protracted, even incapacitating pain. In fact, diabetic patients may constitute 70% of this group (164).

Other complications are related to inappropriate sizing. If the prosthesis is too short, the patient may have an “SST,” or flexion deformity. This can be corrected by dorsal tacking sutures anchoring the glans penis back over the head of the prosthesis (Fig. 42.13). If the prosthesis is exceedingly short, there may be inadequate rigidity in the distal portion of the penis for intromission or disconcerting mobility of the prosthesis. A more subtle problem with more serious consequences is placement of a prosthesis that is too long. This results

in persistent pain, bowing of the penis, and increased risk of eventual erosion.

FIGURE 42.13. Correction of “SST” flexion deformity caused by inserting prostheses that are too short. Nonabsorbable horizontal mattress sutures are placed through the tunica albuginea and the substance of the glans. When tied, the sutures pull the glans back over the tips of the prostheses. (Redrawn from Kaufman JJ, Lindner A, Raz S. Complications of penile prosthesis surgery for impotence. *J Urol* 1982;128:1192.)

A tragic complication of implant surgery is penile gangrene. Two cases have been reported in patients who had pressure dressings applied after surgery, and four other cases

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occurred in diabetic patients, even though no pressure dressings were used (186,229,306).

Inflatable Prostheses

In 1972, Kothari and associates (180) described an implantable fluid transfer system that might be useful in the treatment of impotence. The next year, Scott and associates (312) revolutionized the management of impotence with their report of the implantable inflatable penile prosthesis. Since then, there have been many modifications in the design of the prosthesis and the technique of implantation.

The device consists of two inflatable cylinders: one of which is placed in each corpus cavernosum; a pump that is placed in the scrotum; and a reservoir that is placed extraperitoneally beneath the rectus muscle (Fig. 42.14).

FIGURE 42.14. Scott multicomponent inflatable penile prosthesis. [Redrawn from Reimenschneider HS, Moon SG, Oliver WA, et al. Scrotal implantation of the inflatable penile prosthesis. *J Urol* 1981;126:747 (reference 283).]

Operative Techniques.

The components can be implanted through either a dorsal incision extending from the proximal penis over the pubis or through a penoscrotal incision (Fig. 42.15). The patient is placed in the supine position, and a urethral catheter is inserted. A single midline incision is made in the scrotum just below the penoscrotal junction. The urethra and corpora cavernosa are exposed. Traction sutures are placed in each corpora cavernosum, and a longitudinal 1.5- to 2.0-cm incision is made through the tunica albuginea, exposing the cavernosal tissue. The incision is kept more proximal than distal. A space is developed within the corpus cavernosum extending from the distal subglandular extent to the proximal attachment to the ischium. The space is dilated serially with Hegar dilators. The appropriate penile cylinder length is determined with the Furlow inserter (112). A cylinder is then positioned in each corpus with the inserter. The corporal incisions are closed, and care is taken to have the cylinder tubing exit through the incision at the point at which cylinder and tubing are attached. In cases in which the tubing was juxtaposed with the

cylinder under the tunica albuginea, erosion and leakage occurred. A subdartos scrotal pouch is bluntly developed, on the right for right-handed individuals and on the left for left-handed patients, for placement of the pump. A finger is then placed in the inguinal canal to retract the spermatic cord laterally and to identify the inguinal ligament and the pubic tubercle. Just above the inguinal ligament and adjacent to the pubic tubercle, the transversalis fascia is punctured with dissecting scissors or a right-angle clamp. The puncture site is widened and a space bluntly developed in the perivesical space medial to the epigastric vessels. The empty reservoir is positioned in this space and then filled. In patients who have had previous inguinal or pelvic surgery, such as cystectomy, it is best to place thereservoir in the preperitoneal space under direct vision, usually through a separate inguinal or abdominal incision.

FIGURE 42.15. Placement of the Scott multicomponent inflatable implant. Through a midline scrotal incision **(A)**, the urethra and corpora cavernosa are exposed **(B).** Stay sutures are placed in the tunica albuginea. Through a longitudinal incision, the corporal tissue is dilated, and the corporal length is measured with the Furlow inserter **(C).** The inflatable cylinders are positioned within the corpora cavernosa with the Furlow inserter needle to pass the thread in the tip of the cylinder through the glans penis, providing a means to pull the cylinder into proper position. The corporal incisions are closed so that the cylinder tubing exits directly through the tunica and is not trapped against the cylinder **(D).** Through the inguinal canal, the spermatic cord is retracted laterally and the transversalis fascia is punctured just lateral to the pubic tubercle **(E).** The empty reservoir is pushed through the inguinal canal and through the opening in the transversalis fascia into the perivesical space. The reservoir is filled. The pump is positioned in the scrotum **(F).** The tubing connections are completed and the incisions closed **(G).** (Redrawn from Reimenschneider HW, Moon SG, Oliver WA, et al. Scrotal implantation of the inflatable penile prosthesis. *J Urol* 1981;126:747.)

The pump is situated low in the scrotal pouch so that the deflation valve is lateral, and it is held in place with an externally applied Babcock clamp. Tubing to the contralateral penile cylinder is passed through the scrotal septum to prevent torsion or retraction of the pump. The tubing to all components is then cut to the appropriate length and connected. The intrascrotal tissues just above the pump are closed with absorbable sutures to keep the pump position low in the scrotum. The scrotal incision is then closed with absorbable sutures. The cylinders are left partially inflated.

Antibiotic irrigation is used generously throughout the operative procedure, and systemic preoperative antibiotics are used routinely. The urethral catheter is removed within

1 day. The patients are taught how to operate the pump beginning 3 to 4 weeks after surgery, by which time most pain has disappeared.

Intracorporal Inflatable Prostheses

Intracorporal inflatable prostheses incorporate the advantages of both the semirigid and multicomponent inflatable prostheses. These inflatable implants are completely contained within the corpora cavernosa. These devices function on the principle of transferring a small amount of fluid from a distensible reservoir to a nondistensible chamber. When the fluid is transferred under pressure to the nondistensible chamber, it gives the implant rigidity. Flaccidity is regained by bending the prosthesis to override the pressure threshold

of the release valve. The surgical technique for implantation of these devices is the same as that used for placement of the semirigid implants.

Two-piece Inflatable Prostheses

Two-piece inflatable prostheses consist of cylinders and a combination reservoir and pump. The reservoir–pump is placed in the scrotum (Fig. 42.16). These devices can be placed through either an infrapubic or a penoscrotal incision.

FIGURE 42.16. Two-piece inflatable prosthesis.

Complications.

The inflatable penile implant offers a more physiologic result than the semirigid rod prostheses. Surgical revision rates of up to 43% have been reported (99). The mechanical malfunction rate increases as the length of follow-up is extended, but with continued modification of

the devices, the mechanical failure rates have significantly lessened. There have been relatively few complications with the pumps and reservoirs. However, cases of reservoir erosion into the large bowel and bladder have been reported (193). Most problems have been related to cylinder leaks, aneurysms, or tubing kinks (99,164,168,222). Since the introduction of rear-tip extenders and careful attention to the exit site of cylinder tubing, the incidence of cylinder leaks has decreased (99,223). The incidence of nonmechanical complications, such as infection, is low, and problems with persistent postoperative pain are uncommon (17,168).

Patient and Partner Satisfaction.

The first report on women's reactions to penile implants was published in 1978 by Kramarsky-Binkhorst (181), who interviewed 31 female partners of patients who had previously received a Small-Carrion semirigid penile implant. Less than half (42%) of the women reported that the couple was totally satisfied with the results of the operation; however, a most important observation was made. There seemed to be a direct relationship between perceived success and the level of preoperative consultation and education by the surgeon. In addition, Kramarsky-Binkhorst (181) recognized that the couple's interpersonal relationship was a critical factor in the outcome.

Priapism

Priapism has been clinically defined as a prolonged, painful, penile erection. The disease process is named for Priapus, a Greek god and symbol of good agriculture and hunting who is portrayed as having an enormous phallus. Historically, priapism has been considered to be a low-flow state. A prolonged, painful erection occurs because venous outflow is compromised. Dark blood (with an acidic pH and low Po_2) is typically found on corporal

aspiration and therapy has consisted primarily of surgical shunting procedures designed to improve penile venous drainage. Although high-flow priapism was described more than 40 years ago (51), this second type of priapism has only recently been widely recognized. High-flow priapism is clinically recognizable because the erection is painless and corporal aspiration yields bright red blood. Priapism may be a spectrum disease (204), and the separation of priapism into purely low-flow and high-flow states may be artificial.

Etiology

Low-flow Priapism

Hematologic Causes. One or more priapistic episodes have been reported in 38% to 42% of patients with *sickle cell disease* (87,108). Theories to explain the pathophysiology of priapism in these patients include the relatively acidic state of the corpora during erection, mild acidosis accompanying hypoventilation during sleep, and abnormal endothelial adherence. Paradoxically, four cases of patients with sickle cell disease have been reported with high-flow rather than low-flow priapism (280,333).

The incidence of priapism in *leukemic* patients is less than 1%. Chronic granulocytic leukemia is responsible for 50% of leukemic priapisms (309,336). The cause of priapism in these patients is thought to be hyperviscosity and sludging secondary to high white blood cell counts.

Several reports have convincingly linked *total parenteral nutrition* (TPN) and priapism (89,173). This syndrome has been associated with infusions of 20%, but not 10%, fat emulsions.

Oral Medications. A variety of oral medications, particularly antidepressants and antipsychotic drugs, have been associated with priapism. The highest incidence of priapism is seen with the nontricyclic antidepressant trazodone. Phenothiazines, particularly chlorpromazine, have also been linked to priapism. Priapism has also been associated with several antihypertensive agents, including guanethidine, hydralazine, and prazosin (35). Heparin has also been implicated (174).

Intracavernosal Injection Therapy. Currently, the most common cause of priapism is probably the intracavernosal injection of vasoactive drugs. The incidence of priapism is less with the use of PGE_1 than with papaverine or combinations of papaverine and phentolamine, but priapism has been reported to occur after the injection of only 5 µmg of PGE_1 (308).

Malignant Penile Infiltration. Metastases to the penis may cause priapism. The most common primary tumors responsible for priapism are bladder (30%), prostate (30%), colon (16%), and kidney (11%) (276). The life expectancy of patients with priapism secondary to malignant disease is short.

Neurogenic Causes. Priapism may be seen immediately after high spinal cord injury. Priapism secondary to spinal cord injury usually resolves spontaneously and does not require therapy. Cerebrovascular accidents and other neurologic diseases have been

mentioned as causes of priapism, but such cases are rare.

Idiopathic Priapism. Depending on the patient population, no cause of priapism can be identified in 30% to 50% of cases (274).

High-flow Priapism.

The primary event leading to high-flow priapism is not venous occlusion, but rather high sustained arterial flow (378). The venoocclusive mechanism associated with normal erection is not activated, and the penis remains erect because of unregulated high arterial inflow. Because of high inflow and outflow, hypoxia and acidosis do not develop. The etiology of almost all cases of high-flow priapism is penile or perineal trauma. Injury to the cavernosal artery results in a cavernous artery to corporal tissue fistula (286). Arterial inflow bypasses the helicine arteries and is unregulated. Because the venoocclusive mechanism is not activated, high inflow and high outflow coexist. The number of reported cases of high-flow priapism is limited. In 1994, Bastuba and co-workers (20) added seven case reports to the twelve prior reports of arteriographically confirmed high-flow priapism. Although most reported cases are secondary to external penile or perineal trauma, laceration of the cavernosal artery during the intracorporal injection of vasoactive drugs is a recognized cause of high-flow priapism (20). Cases of high-flow priapism not associated with trauma have occurred. Three patients with sickle cell disease and no history of trauma who presented with high-flow priapism have been reported (280,333).

Evaluation.

A history and physical examination should be performed. Historical findings consistent with a diagnosis of low-flow and high-flow priapism should be sought. Current medications, a history of sickle cell disease, and a history of penile or perineal are particularly important. With high-flow priapism secondary to trauma, there is often a delay from the time of injury to onset of priapism (20). Unlike patients with low-flow priapism, patients with high-flow priapism do not have significant penile pain. Physical examination should include a search for evidence of trauma. In patients with low-flow priapism, the corpora cavernosa are rigid while the glans penis remains soft. The penis in cases of high-flow priapism has been described as being 60% to 100% rigid (44). The patient should be examined for lymphadenopathy and abdominal masses. Initial laboratory studies should include a complete blood count and sickle preparation to rule out leukemia and sickle cell disease as possible etiologies.

Because therapy and the timing of therapy are dictated by whether the priapism is low flow or high flow, aspiration of the corpora should be performed after the initial evaluation. The finding of dark blood indicates low-flow priapism, whereas the finding of bright red blood indicates high-flow priapism. It has suggested that blood gas values of pH less than 7.25, Po_2 less than 30 mm Hg, and Pco_2 greater than 60 mm Hg define ischemic priapism (45). Color duplex scanning has also been advocated (44). This noninvasive study can determine the presence of high-flow priapism and provide information concerning the location of any injury. Angiography is not essential to make the diagnosis of high-flow priapism (20). In most cases, angiography is performed in conjunction with embolization to treat cases of

high-flow priapism.

Therapy.

The differentiation of low-flow from high-flow priapism is important because the treatment of the two conditions is markedly different. In low-flow priapism, therapy is directed at improving venous drainage, whereas in high-flow priapism, the goal is to decrease arterial inflow. Because histologic changes in the penis occur early in low-flow priapism (330), early therapy is indicated. The therapy of high-flow priapism is not an emergency; potency is usually restored after therapeutic intervention, even when the priapism has been present for weeks or months (20).

The therapy of three etiologies of priapism requires special mention. Patients with priapism secondary to metastatic infiltration should generally be managed expectantly. Patients with priapism secondary to leukemia should be treated with chemotherapy and/or penile radiotherapy. Priapism in patients with sickle cell disease is treated initially with hydration, alkalinization, analgesia, and hypertransfusion to increase the hemoglobin to greater than 10 mg/dL and reduce hemoglobin S to less than 30%. If these measures fail, corporal aspiration and instillation of an α-adrenergic agonist can be performed (108,137). Shunt procedures are performed as a last resort in priapism secondary to sickle cell disease.

A diagnosis of low-flow priapism is made when corporal aspiration reveals dark blood. The corpora are then irrigated with saline and an α-adrenergic agonist instilled. The drug of choice is phenylephrine (359). From 100 to 200 μmg is injected (half into each corpora). This dose can be repeated several times with careful patient monitoring and particular caution exercised in patients with preexisting cardiovascular disease. If aspiration, irrigation, and intracorporal α-adrenergic agonist does not result in detumescence, a surgical shunt procedure should be performed. These shunts can be classified as (a) cavernoglanular, (b) cavernospongiosal, (c) cavernosaphenous vein, and (d) cavernopenile dorsal vein. Cavernoglanular shunts are the easiest and fastest to perform. The Winter shunt is performed by excising cores of tunica albuginea between the distal corpora and the glans penis using a Tru-Cut biopsy needle (376). If persistent detumescence is not achieved, an open surgical shunt is indicated. The Ebbehøj and Al-Ghorab procedures

are also cavernoglans shunts. The Ebbehøj procedure consists of a stab wound incision with rotation of the knife blade to create a communication between the corpora cavernosa and the glans. In performing the Al-Ghorab operation, a 2-cm transverse incision is made in the glans penis 1 cm distal to the coronal sulcus (Fig. 42.17) (94). The ends of the corpora cavernosa are identified. and circular incisions are made and a portion of tunica albuginea removed from each corporum. The incision in the glans is then closed with running absorbable suture. Patients who do not achieve detumescence with a corporoglanular shunt require creation of another type of shunt. Grayhack described the use of the saphenous vein to shunt blood from the corpora (Fig. 42.18) (131). The saphenous vein is identified, transected distally, tunneled under the skin, and anastomosed end-to-side to a window created in the tunica albuginea. This procedure, as well as the cavernopenile dorsal vein shunt (19), is technically demanding, and the risk of pulmonary embolus exists. The Quackels cavernospongiosum shunt is performed through a perineal incision (Fig. 42.19)

(278,360). The corpus spongiosum and corpus caverosum are exposed and incised. The shunt is created by suturing the two corpora together, first the inner edge and then the outer edge. This shunt can be performed either unilaterally or bilaterally. This shunt should be performed as far proximally as possible to lessen the chance of urethral injury. Despite early surgical intervention for low-flow priapism, postoperative erectile dysfunction is approximately 50% (33).

FIGURE 42.17. Technique for establishing an Al-Ghorab shunt. (Redrawn from Ercole CJJ, Pontes JE, Pierce JM Jr. Changing surgical concepts in the treatment of priapism. *J Urol* 1981; 125:210.)

FIGURE 42.18. A cavernosaphenous shunt is created by tunneling the transected saphenous vein under the inguinal skin **(A)** and making an end-to-side anastomosis with the corpus cavernosum **(B).** (Redrawn from Grayhack JT, McCullough W, O'Conor VJ Jr, et al. Venous bypass to control priapism. *Invest Urol* 1964;1:509.)

FIGURE 42.19. Creation of a spongiosum-cavernosum shunt. Through a perineal incision **(A)** the corpus spongiosum (midline) and the corpus cavernosum (lateral) are exposed and incised **(B).** The shunt is created by suturing the two corpora together, first the inner edge of the anastomosis **(C)** and then the outer edge **(D).** (Redrawn from Wasmer JM, Carrion HM, Mekras G, et al. Evaluation and treatment of priapism. *J Urol* 1981;125:204.)

In high-flow priapism, the fact that the penis is well perfused argues against immediate intervention. In addition,

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spontaneous resolution has been reported to occur (44). Pharmacologic therapy has been attempted. α-Adrenergic agonists have been used in high-flow priapism in an attempt to decrease arterial flow. Typically, the penis becomes less rigid initially after the injection but then quickly resumes its priapistic state. Both cavernosal artery ligation and embolization have been used in the treatment of high-flow priapism. Ricciardi and co-workers (286) reported two cases of high-flow priapism secondary to trauma; one resolved spontaneously and the other was treated by surgical ligation of the involved cavernosal artery. Two of the four patients treated by Brock and associates (44) underwent an open surgical procedure. Most patients with high-flow priapism have been treated with arterial embolization. This therapy was initially described by Wear (362). The high-flow priapism in all seven cases reported by Bastuba and co-workers responded to this therapy. In two of the three cases reported by Brock, however, angiographic embolization was not successful and open surgical ligation was performed. The use of autologous clot for embolization has been advocated because it permits rapid restoration of blood flow after clot lysis, minimizes complications, and potentially allows for recovery of normal sexual function (356). Absorbable gelatin sponge also produces transient interruption of arterial flow through the lacerated vessels. Because of the small number of reported patients, the possibility of

permanent erectile dysfunction should be explained to the patient prior to therapy.

Peyronie's Disease

Peyronie's disease is a sexually crippling condition of the penis that may result in penile pain, penile curvature prohibiting intromission, and impotence. The mean age of afflicted patients is 53 years, and the clinical course of the disease is variable. The penile curvature is caused by plaque formation secondary to fibrosis of the loose areolar tissue between the tunica albuginea and the corpus cavernosum (327). Light microscopic studies suggest that the plaque originates as a lymphocytic and plasmacytic infiltrate developing in the perivascular spaces of the areolar tissue. Electron microscopic studies corroborate these findings and support the suggestion that there is a process originating as a vasculitis in the tunica albuginea (348). Demyelination of nerve axons has been noted in specimens of plaque, suggesting the potential of neuropathology even before surgery (348). Bacteria have been identified in vascular areas of the tunica albuginea, the vicinity of the urethra, and the periurethral glands, but this is an uncommon finding (36,327), and infection is not considered a primary cause of Peyronie's disease. The vasculitis and inflammatory infiltrates lead to gradual fibrosis that with longer duration eventually compresses the erectile tissue of the corpora cavernosa as the plaque develops. These findings have been confirmed by others who found that in patients with symptoms of less than 6 months' duration, the primary pathologic finding was vascular changes with perivascular infiltration by lymphocytes. In patients with long-term symptoms, biopsy specimens showed no acute vascular changes, but the tissue was rich in fibroblasts (53). Other findings include calcium deposits, bone, cartilage, and even bone marrow formation (327,347). In summary, Peyronie's disease begins as an inflammatory process and progresses to a fibrotic stage, eventually forming a plaque that may mature to bone or cartilage. The plaque is most often located on the dorsum of the penis and may involve the septum between the corpora cavernosa (340). Chesney (63) found multiple plaques in 22% of 250 patients. The plaques most commonly are 1 to 2 cm in width and 2 to 4 cm in length, and penile curvature occurs in 80% to 100% of cases (247).

Even though Peyronie's disease was first described in 1743, its cause is still unknown (75). Numerous factors have been implicated but none proved. Suspected causative factors have included arteriosclerosis, diabetes mellitus, trauma, phlebitis, medications, infections, heredity, or an immune reaction (71,264,267,347,373,382). Bivens and associates (37) reported that 2 of 6 patients with carcinoid syndrome had Peyronie's disease and suggested that elevated levels of serotonin were responsible for the fibrosis found in the retroperitoneum, endocardium, and penises of these men.

Approximately 10% of patients with Peyronie's disease have other types of fibromatoses, such as Dupuytren's contracture, plantar fibromatosis, and fibrosis of the auricular cartilage (36,63), suggesting that an immunologic factor may be involved. Vande Berg and colleagues (347) used scanning and transmission electron microscopy and demonstrated osteoblast-like cells and osteoid formation originating from vascular lumina in areas adjacent to calcified Peyronie's plaques. They suggested that this may result from an autoimmune stimulus associated with some form of vascular trauma. The association between Peyronie's disease and the histocompatibility antigens of the B7 cross-reacting

group suggests that Peyronie's disease may be a pathologic response to an infective agent similar to the B7 antigen. The histocompatibility antigen HLA-B27 has been linked to a variety of fibrosing disorders, particularly ankylosing spondylitis. HLA-B27 also may be related to idiopathic retroperitoneal fibrosis and to the fibrotic changes associated with rotator cuff syndrome (47,374). Noting these relationships, Willscher and colleagues (373) tissue-typed eight patients with idiopathic Peyronie's disease; seven were found to possess an antigen of the B7 cross-reacting group. Citing the suspected immunologic cross-tolerance between HLA-B27 antigen and bacteria of *Klebsiella–Enterobacter* species in patients with ankylosing spondylitis, they suggest that Peyronie's disease may be a characteristic response to a yet unidentified agent that is similar to the B7 cross-reacting group antigens. Nyberg and associates (264) subsequently identified three families with an inherited form of Peyronie's

disease associated with Dupuytren's contracture and the presence of HLA-B27 cross-reacting antigens. Leffell and associates (195) could not substantiate these findings. They phenotyped 28 men with Peyronie's disease for their HLA-A, HLA-B, and HLA-C locus determinants. There was no significant association of any individual B7 cross-reactive antigen or of the B7 antigens considered as a group.

The only reports documenting a specific antecedent agent noted that cessation of β-adrenergic blocking agents (propranolol and metoprolol) resolved the symptoms of Peyronie's disease in several patients (267,382). There is also much uncertainty as to the natural history of Peyronie's disease. The mean age of afflicted patients is 53 years, and the clinical course of the disease is variable. It is self-limited in up to 50% of cases (111) and may resolve spontaneously in 12 to 18 months (56). A retrospective study indicates that the spontaneous resolution rate may not be as high as that previously reported. In a retrospective review of 97 patients followed for 3 months to 8 years, 13% of the patients believed the disease to be one of gradual resolution, 47% believed there had been little or no change, and 40% believed that the disease pattern was one of gradual progression (120).

In 1949, Scardino and Scott (305) suggested vitamin E for the treatment of Peyronie's disease, noting that vitamin E deficiency interfered with the normal repair of connective tissue, resulting in contracture of scar tissue. Even though it has been widely used, the beneficial effects of vitamin E in the management of Peyronie's disease have not been proved. Potassium *para*-aminobenzoate has been a mainstay of therapy for many years, but it is difficult to ascertain any beneficial effect of this agent, and problems with hypoglycemia, nausea, and vomiting have occurred (247,383). In addition, patients find it inconvenient to take 24 tablets daily. Radiation therapy has been reported to be effective in providing pain relief (49,111,143,203,247). With orthovoltage, external radiation therapy complications are essentially nonexistent (111,247). Carson and Coughlin (56) administered doses between 600 and 1,600 rad over a 10- to 90-day period. The average radiation dose was 900 rad. Relief of pain was seen in 78.5%, improvement in the plaque was noted in 13.3%, and penile curvature improved in 6.2%. The average interval to improvement was 5.8 months.

Various other treatments have been used: ultrasound (147), steroid injection (77), topical

β-aminopropionitrile (118), and collagenase injections (119). The plethora of treatments tried in this disease suggests that there is not one that is standard, widely accepted, or predictably efficacious. Also, the natural history is variable; some patients may improve with no therapy, and most authors believe that the results with nonsurgical treatment differ little from those with no treatment (46).

The role of surgery in the management of Peyronie's disease is determined by the severity of curvature or the degree of the patient's disability. A waiting period of from 18 to 24 months after the onset of symptoms until the disease has stabilized is advised (30). The reason why some patients with Peyronie's disease experience erectile dysfunction and others do not is unclear. Venoocclusive dysfunction occurring in the area of the plaque has been suggested (116). In the report of 106 patients by Bystrom and colleagues (53), only 18 were actually impotent but 55 found intromission difficult or impossible because of penile curvature. Early attempts at surgical correction focused on incision of the fibrous plaque (152), but this often resulted in an unstable erection. Subsequent efforts were directed to grafting of the surgical defect with various materials, such as fat, saphenous vein, dermis, or patches of synthetic graft (238).

In 1974, Devine and Horton (79) introduced the use of the dermal graft. After complete excision of the Peyronie's plaque, a dermal patch of exact size was removed from the abdominal wall and sutured into the penile defect with the fat on the inside. They reported good results, and their subsequent experience was also favorable (371). However, Melman and Holland (238) were less enthusiastic. All seven of their patients were completely impotent 1 year or longer after surgery. The cosmetic results of the dermal graft inlay technique were excellent, but they recommended placement of a penile prosthesis to restore a straight phallus and sexual func