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IMPOTENCE FOLLOWING RADICAL PROSTATECTOMY: INSIGHT INTO ETIOLOGY AND PREVENTION

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ABSTRACT

This study was undertaken to identify the cause of impotence in men undergoing radical prostatectomy, with the hope that this information may provide insight into the possible prevention of this complication. The autonomic innervation of the corpora cavernosa in the male fetus and newborn was traced to determine the topographical relationship between the pelvic nerve plexus, and the prostate, urethra and urogenital diaphragm. We have demonstrated that the branches of the pelvic plexus that innervate the corpora cavernosa are situated between the rectum and urethra, and penetrate the urogenital diaphragm near or in the muscular wall of the urethra. Injuries to the pelvic plexus can occur in 2 ways: 1) during division of the lateral pedicle and 2) at the time of apical dissection with transection of the urethra. Thirty-one men who underwent radical retropubic prostatectomy were evaluated to determine risk factors that correlated with postoperative impotence: 5 (16 per cent) were fully potent, 7 (23 per cent) had partial erections that were inadequate for sexual intercourse and 19 (61 per cent) had total erectile impotence. The 2 factors that had a favorable influence on postoperative potency were age and pathologic stage of the lesion: 31 per cent of the patients less than 60 years old were potent versus only 6 per cent of the patients more than 60 years, while 33 per cent of the patients with tumor microscopically confined to the prostatic capsule were potent versus only 5 per cent of those with capsular penetration. When the factors of age and capsular penetration were combined 60 per cent of the men less than 60 years old who had an intact prostatic capsule were potent. Arterial insufficiency and psychogenic factors were excluded as major contributing factors by the finding of normal penile blood flow and absence of nocturnal penile tumescence in the impotent patients. We conclude that impotence after radical prostatectomy results from injury to the pelvic nerve plexus that provides autonomic innervation to the corpora cavernosa. Further studies will be necessary to determine whether refinements in surgical technique, especially during ligation of the lateral pedicle and apical dissection, can prevent this complication.

It is well recognized that radical prostatectomy is effective in curing localized prostatic cancer[1] but since most patients are impotent postoperatively less effective forms of treatment often are used.[2] Inasmuch as postoperative impotence limits the widespread application of radical prostatectomy this study was undertaken to identify possible factors that may lead to impotence. It is hoped that this information may provide insight into the cause and possible prevention of this complication.

Penile erection is a reflex phenomenon, requiring a complex interaction among psychologic, neurologic, hormonal and vascular factors. The primary hemodynamic event leading to penile erection is increased arterial blood flow.[3] The arterial blood supply to the penis is provided by the 2 internal pudendal arteries, which are terminal branches of the hypogastric artery. Although the neural mechanisms involved in increasing penile blood flow are understood poorly 2 distinct pathways exist for the production of erection: 1) a sacral parasympathetic center that is capable of responding to penile or psychic stimulation and 2) a lumbar sympathetic center that is capable of responding to psychic stimuli.[3] These neural pathways pass through the pelvic plexus. However, the exact anatomical course of these nerves as they travel from the pelvic plexus to the corpora cavernosa has not been defined previously. In addition somatic afferent fibers of the pudendal nerve, which do not travel through the pelvic plexus, are necessary to transmit sensory impulses from the penile skin.

The etiology of impotence after radical prostatectomy is unclear, although a variety of potential factors have been cited neurogenic, psychogenic and possibly vascular. We have traced the autonomic innervation of the corpora cavernosa in the male fetus and newborn to determine the topographical relationship between the pelvic nerve plexus, and the prostate, urethra and urogenital diaphragm. These studies were carried out to elucidate how neurogenic factors may be responsible for impotence in patients following radical prostatectomy. In addition, a group of men who underwent radical retropubic prostatectomy was evaluated to determine the prevalence of impotence, to exclude psychogenic and vascular factors that might be responsible and to identify risk factors that correlated with postoperative impotence.

Neuroanatomy of the pelvic plexus. The autonomic innervation of the pelvic organs and external genitalia arises from the pelvic plexus, which is formed by parasympathetic visceral efferent preganglionic fibers that arise from the sacral center (S2 to S4) and sympathetic fibers from the thoracolumbar center (T11 to L2) (fig. 1). The combined parasympathetic nerves enter the plexus via the pelvic nerve (pelvic splanchnic nerve), which was named the nervus erigentes by

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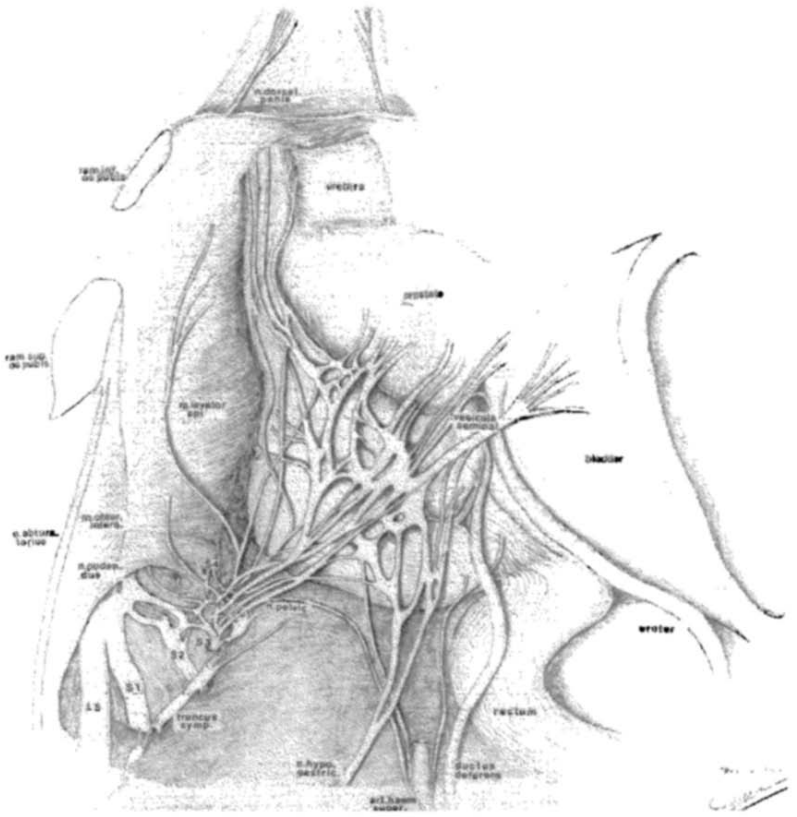

FIG. 1. Dissection of left pelvic plexus in male newborn. Bladder has been retracted to right side. Peritoneum, pelvic vessels, pelvic fascia and pubic symphysis have been removed.

Eckhardt in 1863.[4] This nerve is composed of 5 to 6 separate branches that always originate from the anterior branches of S3 and S4 nerves, and in 12 per cent of the patients from S2 or S5 as well. Their average length is 2.5 to 3 cm.[5] The sympathetic contribution to the pelvic plexus comes from the thoracolumbar center and reaches the pelvic plexus by 3 pathways: 1) the hypogastric nerve (which is the most important), 2) branches from the sacral sympathetic chain (most commonly from the fourth and fifth ganglia) and 3) branches that accompany the superior hemorrhoidal artery (which originate from the autonomic inferior mesenteric plexus). The pelvic plexus in man can be found retroperitoneally beside the rectum and forms a fenestrated rectangular plate, which is situated in the sagittal plane (fig. 1). This plate extends from the sacrum ventrally as high as the pouch of Douglas. Its length is about 4 cm. and its height is 2.5 to 3 cm.

The pelvic nerve courses in the endopelvic fascia and is enclosed in firm connective tissue, which blends with the connective tissue that encloses the hypogastric vessels.[5] The pelvic nerve is found more dorsally than the origin of the branches of the hypogastric vessels, in particular the inferior vesical artery. Consequently, severing of the inferior vesical artery at its origin does not damage the pelvic nerve. However, the branches of the inferior vesical artery and vein, which divide to supply the bladder and the prostate, perforate the pelvic plexus. For this reason, division of the so-called lateral pedicle in its mid portion interrupts not only the vessels but also cuts the nerve supply to the prostate, urethra and corpora cavernosa as well.

The pelvic plexus provides visceral branches that innervate the bladder, ureter, seminal vesicles, prostate, rectum, urethra and corpora cavernosa (fig. 1). Moreover, autonomic fibers innervate the vessels in the pelvic area. Branches that contain somatic motor axons travel through the pelvic plexus and supply the levator ani, coccygeus and striated urethral musculature. The branches to the prostate travel outside the capsule of the prostate and Denonvilliers' fascia until they perforate the capsule when they enter the prostate. The branches to the urethra and the corpora cavernosa also travel outside the prostatic capsule. However, the anatomical course of the branches to the corpora cavernosa has not been described previously. Most of these fibers are extremely small and are difficult to dissect in the adult.[6] Consequently, the destination of these fibers has been traced principally by clinical observations and animal experimentation. Furthermore, because these fibers emanate from a plexus it is impossible to know whether individual nerve fibers are composed of parasympathetic nerves, sympathetic nerves or a combination of sympathetic and parasympathetic elements.[7]

The pudendal nerve is formed by the anterior branches of S2 to S4 and is part of the lumbosacral plexus. It is clear that the pelvic nerve (nervus erigentes) is composed of mainly autonomic parasympathetic fibers, which originate also from the anterior branches of S2 to S4 but take a totally different course from the pudendal nerve. The pudendal nerve does not contribute to the pelvic plexus but leaves the pelvis through the lower part of the greater sciatic foramen, crosses the spine of the ischium and re-enters the pelvis through the lesser sciatic foramen. It accompanies the internal pudendal vessels along the lateral wall of the ischiorectal fossa and splits as it approaches the urogenital diaphragm into 3 terminal branches: 1) the inferior hemorrhoidal nerve, 2) the perineal nerve and 3) the dorsal nerve of the penis. The dorsal nerve of the penis is the terminal deeper branch of the pudendal nerve that accompanies the internal pudendal artery along the ramus of the ischium and then runs forward along the margin of the inferior ramus of the pubis, lying between the superficial and deep layers of fascia of the urogenital diaphragm. After piercing the superficial fascia it gives branches to the corpora cavernosa penis and runs along

the dorsum of the penis, distributing sensory fibers to the skin, and terminates at the glans penis. Penile sensation is transmitted along the sensory portion of the pudendal nerves. Autonomic fibers are enclosed in the pudendal nerve, parasympathetic as well as sympathetic. The latter join the anterior branches of S2 to S4 by means of rami communicantes from the ganglia in the sacral sympathetic chain.

Recognizing that the branches of the pelvic plexus that innervate the corpora cavernosa pass through the urogenital diaphragm and that injury to these nerves may be responsible for impotence following radical prostatectomy we have attempted to trace their pathway. To investigate this course initially sections of fetal material were studied. A male fetus of 11 cm. crown-rump length (that is about 4 months of gestation) was sectioned transversely in a series of 10 μ. thickness and stained with AZAN (azokarmin B anilinblau W). In earlier investigations it was shown that the prostatic and membranous urethra received branches from the pelvic plexus but not from the pudendal nerve or dorsal penile nerve.[8] When the branches that supply the corpora cavernosa are followed in these sections it can be seen that they run immediately adjacent to and through the wall of the membranous urethra as they exit through the urogenital diaphragm and pass close to the glands of Cowper, which they innervate as well, before they enter the dorsal medial side of the corpora cavernosa (fig. 2). Every twentieth section of this area was drawn and from these drawings a composite illustration was made in 3 dimensions (fig. 3). This illustration demonstrates that in this specimen the course of the nerves to the corpora cavernosa pass through the urethral wall. In another specimen of 20 cm. crown-rump length (6 months of gestation) the same method was used and a composite drawing was made (fig. 4). This illustration demonstrates that the nerves to the corpora cavernosa come from branches that are

FIG. 2. Transverse section through male fetus 11 cm. crown-rump length. Course of nerves to corpus cavernosum through urethral wall are demonstrated. *1*, bulbous urethra. *2*, left corpus cavernosum. *3*, left pubic bone. *4*, left dorsal penile nerve. *5*, right dorsal penile nerve. *6*, branch of pelvic plexus to corpus cavernosum. *7*, membranous urethra.

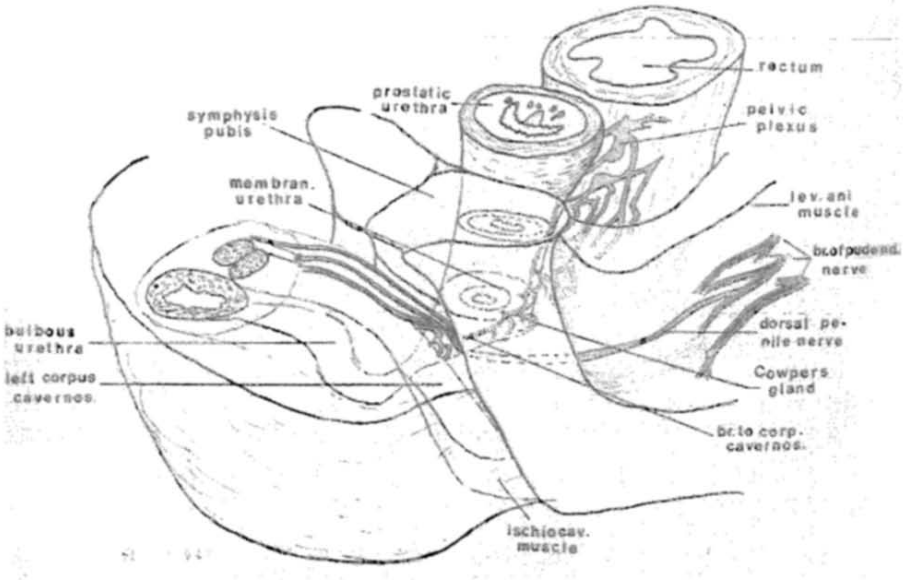

FIG. 3. Male fetus 11 cm. crown-rump length, composition of microscopic sections

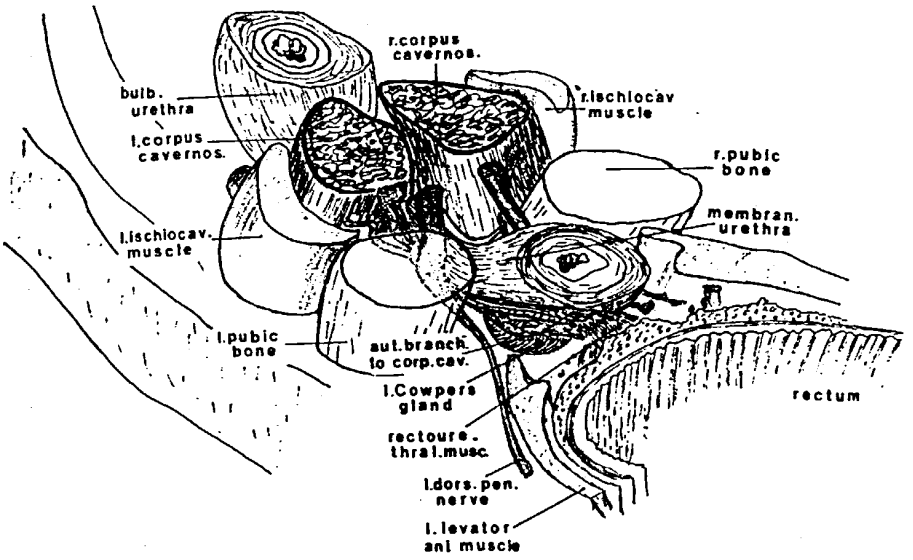

FIG. 4. Male fetus 20 cm. crown-rump length, composition of microscopic sections

situated between the rectum and the urethra, just cranial to the rectourethralis muscle. In this specimen the nerves did not run in the wall of the urethra but closely beside the muscular wall of the membranous urethra. However, the nerves always followed closely near the urethra when they traversed the urogenital diaphragm.

As mentioned previously dissection of the pelvic plexus in the adult is difficult. However, this dissection is easier to perform in the newborn because the connective tissue and fat are looser, and can be removed more easily from the nerves and vessels. Besides, the nerves in young individuals are relatively thicker than in adult material. Dissections were done with a dissecting microscope under a magnification of 6 to 10 power in a 1-month-old infant and a male newborn. A bundle of nerves courses on the left dorsolateral side of the urethra between the rectum and the urethra (fig. 5). These nerves supply branches to the urethra and then travel through the urogenital diaphragm, where they pass behind the dorsal penile artery and the dorsal penile nerve before they enter the corpus cavernosum penis.

Evaluation of sexual function following radical retropubic prostatectomy. We evaluated 31 men who had undergone radical retropubic prostatectomy for clinical stage B1 disease. All patients were potent preoperatively and all operations were performed by the same surgeon using techniques described previously.[9,10] Evaluations were performed at least 6 months postoperatively and included careful interviews, stamp nocturnal penile tumescence testing performed on 3 consecutive nights[11] and penile blood flow studies (penile/brachial index).[12] The 5 patients who had undergone prior placement of a penile prosthesis were classified as impotent and the latter 2 studies were not performed.

Of the 31 men who underwent radical retropubic prostatectomy 5 (16 per cent) were fully potent postoperatively. All of these patients had the ability to achieve psychogenic erections and vaginal penetration with orgasm, and all had normal nocturnal penile tumescence studies. Seven patients (23 per cent) reported that they had partial erections that were inadequate for sexual intercourse and all 7 had positive nocturnal penile tumescence studies. Nineteen patients (61 per cent) had total erectile impotence and all had negative nocturnal penile tumescence studies. Of the 26 men who could not achieve vaginal penetration 25 (93 per cent) reported that they experienced orgasm with manual stimulation. Seven patients (26 per cent) underwent placement of a penile prosthesis.

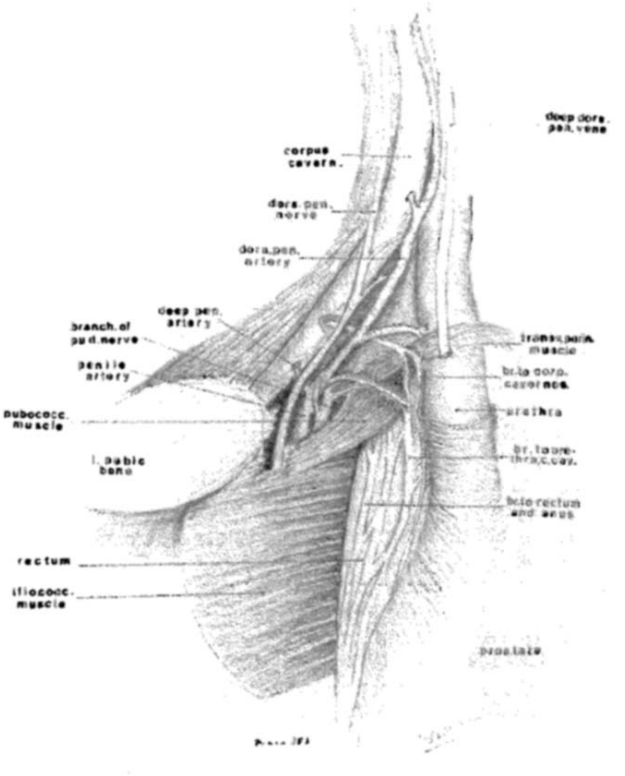

FIG. 5. Dissection of caudal and ventral part of left pelvic plexus in male newborn. Pubic symphysis, vessels and endopelvic fascia are removed. Lateral part of urogenital diaphragm is separated from pubic bone.

The mean age of all patients was 60 years (range 45 to 68 years). The median ages of the potent patients, and those with partial and absent erections were 58, 62 and 64 years, respectively. Of the 5 patients who were potent 4 (80 per cent) were <60 years old, while of the 7 patients with partial erections and 19 with absent erections only 2 (29 per cent) and 7 (37 per cent), respectively, were <60 years old. When the data are analyzed in another way 31 per cent of the

Factors associated with potency in men following radical retropubic prostatectomy

Factor	Total No.	No. Potent (%)
Age (yrs.):		
<60	13	4 (31)
>60	18	1 (6)
Capsular penetration:		
Intact	12	4 (33)
Penetrated	19	1 (5)
Age (yrs.) and capsular penetration:		
<60, intact	5	3 (60)
<60, penetrated	8	1 (13)
>60, intact	7	1 (14)
>60, penetrated	11	0 (0)

patients who were <60 years old were potent versus only 6 per cent of the patients >60 years old (see table). When pathologic findings were correlated with postoperative potency it was found that only 1 of the patients who was potent had microscopic penetration of the prostatic capsule. In this patient the lesion was located at the base of the prostate, well away from the membranous urethra and urogenital diaphragm. When the factors of age and capsular penetration were combined it appears that 60 per cent of the patients <60 years old who had an intact prostatic capsule were potent. Indeed, the only 2 patients in this group who were impotent had lesions that were located at the apex of the prostate, near the membranous urethra and urogenital diaphragm. Penile blood flows were performed on 7 of the impotent patients. In all cases the penile/brachial index was normal[12] (mean 0.89 ± 0.09 standard deviation, range 0.75 to 1.0).

DISCUSSION

In most series in which information is provided about sexual function after radical prostatectomy potency ranges from 0 to 10 per cent.[13–17] However, Finkle and associates have reported more encouraging results with potency rates of 43 to 60 per cent.[18,19] In our series 16 per cent of the patients were potent and another 23 per cent had evidence of nocturnal erections. However, in the latter group erectile function was inadequate for vaginal penetration. Although these patients may have psychogenic impotence it is our opinion that they have a less severe organic component than the 61 per cent of patients who were totally impotent. In attempting to determine why most patients were impotent after radical prostatectomy one must question why 5 patients were potent. What is the reason for the success in these cases? A variety of possibilities could explain this finding: subtle differences in surgical technique, lack of tumor extension beyond the capsule, thus, reducing extensive periprostatic dissection, or subtle variations in anatomy. In this series all procedures were performed by the same surgeon, thus, reducing variability introduced by technique. The 2 factors identified in this study that appear to have a favorable effect on potency were age and capsular penetration. Indeed, in patients <60 years old who had tumor confined within the prostatic capsule 60 per cent were potent. The only 2 patients with this finding who were not potent had apical lesions located near the membranous urethra and urogenital diaphragm, where injury to the branches of the pelvic plexus is most likely. Although it is easy to see how pathological factors would influence potency it is unclear why patients <60 years old were potent more often than those patients who were older. A similar finding has been reported by Finkle and Taylor.[19] Although this finding can be attributed to the fact that younger men are interested more often in sexual function it also is possible that because the prostate in younger men is smaller the likelihood of injury to the branches of the pelvic plexus that travel adjacent to the prostate is lessened. In future studies estimates of prostatic volume should be made to evaluate this possibility further.

The finding of normal penile blood flow in impotent patients suggests that arterial insufficiency is not an important factor. This is not surprising because the hypogastric artery was not ligated during the procedure. Although the dorsal vein of the penis was always ligated it appears that disruption of the venous drainage to the penis does not interfere with sexual function.[20]

Based on these findings we conclude that impotence following radical prostatectomy results from injury to the pelvic plexus that provides autonomic innervation to the corpora cavernosa. This injury can occur in 2 ways: 1) when the lateral pedicle is divided during removal of the prostate and tissue adjacent to the gland the main pelvic plexus can be injured, resulting in damage to the nerves that innervate the prostate, urethra and corpora cavernosa, and 2) injury can be inflicted during apical dissection of the prostate and transection of the urethra and its surrounding tissue. During this maneuver only those nerve bundles that specifically innervate the corpora cavernosa will be injured. Because the pudendal nerve and the dorsal penile nerve are not injured penile sensation and orgasm are retained following radical prostatectomy. It is difficult to understand why injury to the small pelvic nerves that traverse the urogenital diaphragm induce impotence when the autonomic supply provided by the pudendal nerve,[21] which is large, remains intact. However, it is possible that the nerves that originate from the pelvic plexus and pass through the urogenital diaphragm specifically innervate the corpora cavernosa, whereas the fibers that travel with the pudendal nerve innervate only the vessels. There is a clinical correlation that supports these findings. It is well known that injury to the membranous urethra induces impotence. This injury occurs in patients with pelvic fractures who have urethral disruption[22] and in some patients following transurethral sphincterotomy when it is performed laterally at the 3 and 9 o'clock positions.[23–25] This supports the notion that the autonomic branches to the corpora cavernosa are associated intimately with the membranous urethra and travel dorsolaterally next to its wall.

When a radical perineal prostatectomy is performed the prostate is approached inside the striated anal sphincter along the rectal wall after the rectourethralis muscle is incised. When the rectum is freed from the urethra it is almost impossible to prevent severing the nerves to the corpora cavernosa. Even during perineal exposure of the prostate for open biopsy or simple perineal prostatectomy, in which cases the dissection is more limited, impotence can be induced.[26] Presumably this results during lateral dissection with traction on the delicate branches of the pelvic plexus which are stretched between the rectum and the anteriorly displaced prostate. Phifer, the famous Chicago perineal surgeon who performed >100 simple perineal prostatectomies yearly, confined his dissection as close to the midline as possible and avoided the use of lateral retractors. He thought that "the wider you expose the prostate for the audience, the more likely the patient will be impotent."

In contrast to perineal exposure of the prostate, during radical retropubic prostatectomy the anatomical relationship among the branches of the pelvic plexus, urethra, rectum and rectourethralis muscle is not disturbed. Consequently, in the future it may be possible to preserve the nerves adjacent to the membranous urethra by dissecting closely along or even through the muscular wall of the urethra before it is transected. Accurate ligation of the dorsal vein complex is desirable before apical dissection to provide a bloodless field during this important dissection.[10] After this maneuver the apex of the prostate can be separated from the rectum in the midline to expose the posterior surface of the prostate. If one is treating tumors that are truly confined to the prostate, without penetration of the capsule, the dissection can then be

performed immediately adjacent to the capsule without extensive lateral dissection. The pedicle should be ligated as close to the prostate as possible to avoid injury to the pelvic plexus. Experience with this technique will be necessary to determine whether the effectiveness of the procedure will be jeopardized by these maneuvers and whether the chances for potency will be increased. These same principles are applicable to cystoprostatectomy for the treatment of invasive bladder cancer. Although impotence almost always follows radical cystectomy Bergmann and Young have avoided impotence in this setting by "coring out" the prostate and leaving only the apical prostatic capsule.[27] Of 10 patients so treated 9 were potent, which suggests again that injury to the nerves during dissection of the membranous urethra may be the cause of impotence in men undergoing cystoprostatectomy.

In summary, we have attempted to identify the cause of impotence in patients undergoing radical prostatectomy with the hope that this knowledge might lead to its prevention. This is our first report on the subject and much remains to be learned. Based on the findings in this study it is unlikely that potency can be maintained in men with locally extensive disease with capsular penetration. Rather, the principles outlined seem to be more applicable to patients undergoing prostatectomy at the time of cystectomy or to patients with organ-confined prostatic cancer. Recognizing that radical prostatectomy is more effective than external beam radiation therapy in the management of localized prostatic cancer,[1,2,28] it is incumbent upon urologists to perfect surgical techniques so that fears about the morbidity of the procedure do not discourage patients and physicians from selecting the optimal form of treatment. In this study 60 per cent of the patients who were <60 years old and who had tumor microscopically confined to the prostate were potent postoperatively. With further refinements in surgical technique it may be possible to improve this record. If so, fears about impotence may be dispelled and physicians may take a greater interest in diagnosing prostatic cancer in young men at an early stage when it is still curable.

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