The innervation and function of the lower urinary tract

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Vesical and urethral function are closely controlled by neural activity, both reflex and volitional. Relatively subtle abnormalities have serious consequences. Understanding of the natural history of neurogenic vesical dysfunction has improved over the past few years and is summarized in this review article.

KEY WORDS • urinary tract innervation • urinary function • nervous system

In the past 10 years, our concepts regarding neurogenic lower urinary tract dysfunction have undergone some fundamental changes. Traditional urological methods of management were based on providing prompt urinary drainage using urethral catheters, suprapubic tubes, surgical incision of the urethral sphincters, and urinary diversion. The introduction of intermittent catheterization and a better understanding of the normal mechanisms involved in low-pressure urinary storage and periodic low-pressure urinary expulsion by the bladder have led to changes in urological methods of treatment for patients with either central or peripheral neural lesions.

Anatomical Description

Innervation of Lower Urinary Tract

The lower urinary tract consists of the bladder, which is composed of bundles of the detrusor musculature, and the urethra which contains a dual sphincter mechanism. The bladder can be divided into a base and a body at the entry point of the ureters. The base below the ureters has abundant alpha adrenergic innervation and contains the trigone which receives the ureters. The response of the bladder base to filling and pharmacological manipulation is similar to that of the urethral smooth musculature and is reciprocal to the responses of the bladder body which lies above the entry point of the ureters.

The urethral sphincter mechanism has two parts: an internal and an external sphincter. The smooth-muscle sphincter of the urethra, which is involuntary, extends from the bladder outlet through the pelvic floor. It consists of circular and longitudinal smooth musculature with both adrenergic and cholinergic innervation (Fig. 1). Despite anatomical data that indicate the lack of a true anatomical sphincter at the bladder neck, urine is in fact held at the vesical outlet. This sphincter mechanism can be weakened by sympathectomy or the administration of alpha adrenergic blocking agents.

During bladder filling, the internal sphincter is closed by the activity of adrenergic neurons. The external urethral sphincter has two components, of which one is intrinsic to the urethra and lies completely within the urethral wall and the other is extrinsic to the urethra and is formed by the skeletal muscle fibers of the pelvic floor and urogenital diaphragm. The intrinsic sphincter, which lies within the urethra proper, extends superiorly from the pelvic floor for a variable distance. Anteriorly, some skeletal fibers reach as far as the bladder neck.

The intrinsic part of the distal sphincter mechanism is composed of slow-twitch musculature and may have both autonomic and somatic innervation.

Nonspecialized sensory endings are localized within the bundles of the detrusor and urethral smooth musculature. During bladder stretch, sensory neural activity can be recorded from the pelvic nerve and the second and third sacral roots. The major pathway for reflex responses to filling, including both storage and...
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**FIG. 1.** Schematic diagram of the urethral sphincter. The smooth-muscle closing mechanism extends from the vesical outlet to the pelvic diaphragm. The skeletal sphincter is composed of fast-twitch musculature, extrinsic to the urethra which receives pudendal (somatic) innervation. The intrinsic skeletal musculature probably does not have pudendal innervation, and is not part of the pelvic floor.

micturition reflexes, involves the sacral roots and pelvic nerve. There are also no specialized sensory receptors within the intrinsic part of the external sphincter. The extrinsic sphincter portion consists of pelvic floor musculature that has spindle receptors and typical somatic motor neuron end plates. The pudendal nerve provides motor innervation to the extrinsic skeletal sphincter. The source of the somatic motor fibers to the intrinsic part of this skeletal sphincter has not been established, but it does not appear to be via the pudendal nerve. A remaining question regarding the slow-twitch intrinsic part of the distal sphincter mechanism is whether it behaves like the pelvic floor below it or like the urethral smooth sphincter above. From available clinical and experimental evidence, it appears to behave like the smooth-muscle sphincter above in terms of continence but may act in concert with the pelvic floor in some circumstances.

**Motor Innervation of Detrusor Muscle and Urethral Smooth Muscle**

The pelvic ganglia lie in the outer part of the bladder wall close to the ureteral entry zone. They receive preganglionic input from the thoracolumbar and sacral spinal cord. Postganglionic neurons are both cholinergic and adrenergic, and innervate the detrusor and urethral smooth musculature. Despite a common innervation, the bladder base and urethral smooth sphincter behave differently than the bladder body in response to pharmacological agents and neural stimulation. During vesical filling, the body relaxes and the urethra increases contractility; during micturition, the body contracts and the urethra relaxes. There are, in addition, a number of demonstrated interactive processes involving cholinergic and adrenergic neurons within and distal to the pelvic ganglia. These include an inhibitory effect on cholinergic ganglionic transmission by preganglionic sympathetic discharge during vesical filling and an inhibitory effect on adrenergic stimulation of the urethral smooth musculature by parasympathetic discharge at and distal to the pelvic ganglia, which can be demonstrated by selective sacral root stimulation.

**Spinal Innervation of Detrusor and Urethra**

The neurons innervating the detrusor and skeletal sphincter are found in the conus medullaris. The detrusor motor cells are located in the intermediolateral cell columns of the S2–4 cord segments. Nerve block studies indicate that the innervation of the detrusor may be asymmetrical. The pudendal motor neurons innervating the external sphincter and pelvic floor have been localized to Onuf’s nucleus in the anterior horn of the sacral cord segments. Clinically, lesions of the sacral spinal cord or the sacral roots are much more likely to result in total loss of detrusor innervation than total denervation of the external sphincter. It remains to be proven in man whether this effect of a sacral cord or sacral root lesion is due to a peculiar dual innervation of the intrinsic part of the external sphincter (which has been established in the cat).

The intermediolateral cell columns of the T-10 through L-1 or L-2 cord segments contain the neurons concerned with sympathetic innervation of the bladder and internal urethral sphincter, and the “genital sphincter” in males.

**Organization of Reflex Activity Serving Lower Urinary Tract Function**

Specific information in man regarding ascending and descending spinal pathways and supraspinal activity as it relates to lower urinary tract function is not available. What is known is largely a result of inferences drawn from the study of patients with known lesions, and what follows is a summary of the available information.

**Spinal Micturition Center.** There does not appear to be a true spinal micturition “center.” Suprasacral spinal cord transection in man, in the non-human primate, and in the cat results in the loss of the normal sequence of reflex events during bladder filling and micturition. Following supraspinal cord injury, external sphincter activity does not increase during filling but rather increases at the time of a bladder contraction and is short in duration. Patients with lesions above the T-5 level show a heightened sympathetic response to filling and micturition, which may
progress to the syndrome of autonomic dysreflexia. This syndrome consists of a massive sympathetic response to afferent stimuli: usually related to bladder filling, micturition, or rectal distention. Other symptoms are increased blood and pulse pressures, bradycardia, a pounding occipital headache, sweating, and sometimes vasomotor skin changes above the spinal neural lesion. These findings in man with spinal cord injury suggest that the “center” for lower urinary tract function is supraspinal. The experimental findings of De Groat⁶ indicate that afferent activity generated by bladder filling projects directly to the brain stem in the cat. A similar process may occur in man.

Patients with lesions above the brain stem (for example in the internal capsule) typically show precipitant low-volume micturition but normal reflex responses to filling as well as coordinate bladder and external urethral sphincter activity during micturition. In contrast, patients with spinal cord injuries show abnormal reflex responses to filling in addition to uninhibited micturition.¹² These findings indicate that the center for lower urinary tract functional integration is supraspinal, probably in the brain stem (Fig. 2). There is some indirect evidence that suggests that in man the center is not pontine, but the evidence is incomplete.

Volitional control of reflex micturition appears to be superimposed on a complex group of reflex events that moderate the detrusor response to filling. The latter reflex processes are poorly understood and characterized. However, the abnormalities encountered in patients with Parkinson’s disease, for example, provide some indirect information on the role of the basal ganglia in bladder function. These patients typically show uninhibited detrusor contractile responses and short-duration bladder contractility associated with residual urine formation.

There is some experimental evidence that basal ganglionic activity increases with bladder filling and ceases during micturition.¹⁶ While these findings suggest some contribution by the basal ganglia to reflex vesical function, the precise contribution has not been clearly established. Presumably, any such influence would be exerted via extrapyramidal pathways. Inhibitory volitional influences on detrusor contractility appear to be exerted principally on the pudendal neurons, the activity of which results in inhibition of the detrusor neurons in the sacral spinal cord. While this may not be the only site of inhibition (which could for example occur within the brain stem, where detrusor “inhibitory” and “facilitatory” centers have been described experimentally), it is the only site clearly identified in man.¹⁵

**Lower Urinary Tract Function.** Bladder and urethral muscle behavior are normally reciprocal. During bladder filling or storage of urine, the bladder pressure remains low while urethral pressure increases. During micturition, bladder pressure rises and urethral pressure is lowered.¹⁸ The increase in bladder volume, which occurs with very little increase in bladder pressure, was formerly attributed solely to the properties of the bladder wall, but it is now clear that reflex neural activity is essential to low-pressure storage of urine (Fig. 3). Pelvic nerve, sacral cord, and sacral root lesions interfere directly with low-pressure bladder storage of urine.¹⁸ Experimental transection of the pelvic nerve or sacral roots or ablation of the sacral cord results in an abnormally steep pressure response by the bladder to increasing volume. During bladder filling, urethral resistance remains fixed.²⁵,³¹ These rather subtle abnormalities have important clinical consequences. Since bladder pressure rises with filling, as bladder pressure approaches urethral sphincter resistance urinary leakage occurs. Bladder pressures above 40 cm H₂O, if sus-

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**Fig. 2.** Schematic diagram of the putative spinal and supraspinal organization of neural activity that controls lower urinary tract function. Sensory information evokes a brainstem response which initially is inhibitory to the detrusor. The inhibition may take place within the brain stem and is also directly associated with increased skeletal sphincter contractility driven by increasing pudendal nerve activity. There also appears to be a supraspinal response that increases thoracolumbar autonomic neural activity that is in turn associated with relaxation of the detrusor smooth muscle and constriction of the urethral smooth muscle. Cortical inhibitory influences on the detrusor are indirect and appear to be exerted on the pudendal neurons which activate detrusor inhibition as a by-product of constriction of the pelvic floor. There are apparently other areas involved in detrusor modulation but they are incompletely characterized.
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Since these changes in the normal reflex responses to bladder filling occur after a loss of pelvic nerve integrity, as well as sacral cord or sacral root injury, it is reasonable to conclude that, normally, sensory activity excited by bladder filling is carried by the pelvic nerve and leads to central neural activity that results in inhibition of detrusor contractility and facilitation of bladder relaxation. Experimentally, sympathetic neural responses to afferent pelvic nerve firing associated with increasing bladder volume have been demonstrated: 1) beta receptor-mediated relaxation of the detrusor muscle;3,10 2) an alpha receptor-mediated increase in urethral smooth-muscle activity and urethral pressure;46 and 3) inhibition of ganglionic transmission in the pelvic (vesical) ganglia, which, in effect, inhibit the sacral parasympathetic outflow to the bladder.27 In addition to sympathetic activity, afferent nerve activity during bladder filling results in increased pudendal nerve activity and increased contractility of the external sphincter and pelvic floor. These responses have been shown to both increase urethral sphincter pressure and inhibit preganglionic detrusor motor neurons in the intermediolateral cell columns of the sacral spinal cord50 (Fig. 3). Experimentally, after suprasacral spinal cord injury, the detrusor external sphincter relationship which is expressed by pelvic afferent and pudendal efferent neural activity is disordered, out of sequence, and sometimes antagonistic.23 These findings are identical to those seen in man after suprasacral spinal cord injury, which suggests that suprasacral centers are involved in the normal reflex responses to bladder filling. Similarly, after a very high-level spinal cord injury in man, non-human primates, and cats, sympathetic responses to bladder filling are late, disorderly, and very markedly heightened.27,32 The clinical syndrome of "autonomic dysreflexia" can be eliminated by low spinal anesthesia, sacral cord or sacral root blockade, or topical bladder anesthesia. These findings indicate that the major pathway for reflex activation of sympathetic responses to vesical filling is the pelvic nerve. It also suggests that reflex neural activity cranial to the sacral and thoracolumbar spinal cord is required for normal parasympathetic and sympathetic neural responses to filling.

Normally, both urethral smooth muscle and skeletal muscle respond to filling with an increased contraction, measurable as an increase in urethral pressure and urethral skeletal sphincter activity demonstrated by electromyography (EMG). After pelvic nerve transection, urethral pressure responses to bladder filling disappear and urethral pressure remains fixed.

Smooth-Muscle Component of the Urethral Sphincter

The urethral sphincter mechanism is complex and there is no universally accepted explanation of its function. It appears that smooth muscle of the urethra is at least partially innervated by sympathetic nerve fibers. This "primary" sphincter extends from the bladder to the area most closely associated with skeletal muscle activity and probably into that structure. The evidence for sympathetic innervation is quite good. Loss of thoracolumbar activity after spinal cord infarction results in loss of urethral smooth-muscle closure of the bladder neck and proximal urethra, as does the administration of alpha synthetic blocking agents or peripheral sympatheticectomy.19,21,29,43 These urethral changes need not be accompanied by loss of sacral cord reflex function or parasympathetic nerve-mediated reflex detrusor activity. There are parasympathetic receptors present in urethral smooth muscle, which presumably have an influence on urethral function.7,14 The precise nature of that influence is not clear, although it is more likely to be an effect on the urethra at the time of micturition than on closure of the urethra during bladder filling, since the latter aspect of urethral function is clearly maintained after sacral cord or sacral root ablation.2 A wide-open incompetent urethral sphincter mechanism is reasonable evidence of a sympathetic neural injury or lesion (Fig. 4).

Normal Function

Skeletal Urethral Sphincter Function

The portion of the pelvic floor which the urethra traverses surrounds and compresses the urethra. The pelvic floor musculature is composed of fast-twitch fibers innervated by the pudendal nerve. Contraction of the external sphincter is the mechanism used by man, the non-human primate, and the cat to control reflex detrusor activity (Fig. 5). Experimentally, stimulation of the pelvic floor results in inhibition of detrusor contractility. This effect can be elicited in primates with
Fig. 4. Radiograph showing a nonfunctioning internal sphincter in a child with myelodysplasia. There is function of the distal sphincter, which is associated with some electromyographic activity recorded from the pelvic floor (arrow). At present, there is no method of determining whether this is the "extrinsic" or "intrinsic" part of the sphincter.

Lower Urinary Tract Function at Urination

At some point during bladder filling, a reflex threshold in the brain stem is broached and micturition occurs. This process involves a fall in urethral pressure and a rise in bladder pressure which persists until bladder emptying occurs. The evidence that the reflex center for this activity is supraspinal is substantial. Decerebration in the cat does not adversely influence reflex micturition, but destruction of the pons and of the brain stem permanently abolishes it. For a time after suprasacral spinal cord injury, the cat, the non-human primate, and man lose reflex bladder activity which later returns after recovery from spinal shock. In none of these species is reflex urinary tract function normal after spinal cord injury. The bladder reflexly contracts at a lower volume than normal, and bladder contractility is discoordinate with external sphincter activity and typically does not continue until the bladder is emptied. Little or no "guarding" reflex EMG activity from the pelvic floor is generated during bladder filling, but instead pudendal nerve-mediated external sphincter EMG activity and external sphincter-derived pressure increases dramatically with bladder contractility (Fig. 5). Sympathetic responses to bladder filling are often heightened and persist during bladder activity. None of these abnormalities occur in patients with lesions superior to the brain stem, in whom the major abnormality is sudden unanticipated reflex vesical contractility that is difficult or impossible to halt. These findings allow the inference that the reflex center for both storage and micturition is supraspinal. The center is thought to be pontine in cats, but it may be lower in man.

Abnormal Function

Spinal Cord Lesions

Abnormalities of lower urinary tract function after a suprasacral spinal cord injury are clinically expressed as incontinence, residual urine retention, elevated storage and micturition pressures, and infection (Fig. 7). Ultimately, this can lead to upper urinary tract dilatation, vesicoureteral reflux, upper tract infection, stone formation, and finally renal parenchymal destruction. These processes are not substantially altered by either urinary diversion procedures or catheter drainage since both have high complication rates, especially infection; however, long-term outcome is clearly improved by sphincterotomy for drainage in males with high-pressure discoordination between the bladder and external sphincter.

It is clear that the measure of risk in lower urinary tract dysfunction after spinal cord injury is not residual urine but intravesical pressure. Provided the pressure of reflex vesical activity is low (35 cm H2O or less) or can be made low by using anticholinergic agents, rhizotomy, or augmentation cystoplasty, upper urinary tract changes will not occur. Intermittent catheterization as a permanent method of management of spinal cord injury patients works well if vesical storage activity is reasonably normal. The decision to proceed with sphincterotomy or to maintain patients on intermittent
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![Diagram of bladder pressure and pelvic floor EMG](image)

**Fig. 6.** Upper: Urodynamic tracing during normal micturition in a 9-year-old child, measured by bladder pressure and a pelvic floor electromyography (EMG). The initial voluntary response is a cessation of EMG activity, followed by a sustained elevation in bladder pressure which normally does not exceed 30 cm H2O. Lower: Tracing obtained during reflex micturition in a 20-year-old paraplegic with a T-4 sensory level. With the onset of high bladder pressure, there is an inappropriate discoordinate increase in EMG activity, which is obstructive in character. Intravesical pressures are high, and "voiding" is poor.

Catheterization can be based on the bladder pressure. If the bladder will not store urine without contracting or exhibiting a rise in pressure to 40 cm H2O, then some method to decrease bladder outlet resistance and allow urinary leakage at low pressure is indicated in males. In practice, this occurs in about 30% of male patients with spinal cord injury, although some quadriplegics cannot be managed with intermittent catheterization and require total sphincterotomy to permit passive urinary drainage into a condom collection system. Females tolerate catheters better than males; however, over time, bladder calculi, pyelonephritis, reflux, vesicourethral erosion, renal stone formation, and loss of renal function occur in over 50% of female patients. Since females cannot be treated by external sphincterotomy and condom collection, a vigorous attempt to stop reflex vesical activity with drugs, augmentation cystoplasty, or rhizotomy is indicated to preserve low-pressure storage function and permit intermittent catheterization.

**Suprasacral Spinal Cord Lesions and Autonomic Dysreflexia**

The syndrome of autonomic dysreflexia potentially occurs in any individual with a lesion superior to T-5 but is a practical problem only in patients with cervical lesions. In most instances, the syndrome results from bladder filling, reflex bladder activity, or bowel distention, but it can arise from a somatic focus and may be postural and/or associated with a large pressure ulcer. It commonly occurs relatively early after spinal cord injury in patients managed by intermittent catheterization. This kind of dysreflexia associated with increased bladder volumes can be controlled with small doses of prazosin, 1 mg/24 hrs, or chlorpromazine, 10 to 25 mg/12 hrs.

Sustained autonomic dysreflexia is common in patients with suprapubic tubes and small contracted bladders. These patients are best managed with daily doses of alpha blocking agents and should be treated with parenteral chlorpromazine prior to a catheter change if that is known to precipitate autonomic dysreflexia. Uncontrollable autonomic dysreflexia may occasionally require a sacral rhizotomy if the irritative focus cannot be treated. Sustained autonomic dysreflexia due to an untreatable condition or a condition that cannot be treated immediately can be temporarily abated by intravenous bolus injections of phentolamine mesylate, 5 mg, interspersed with small intravenous doses of chlorpromazine, 1 to 2 mg, until blood pressure gradually returns to normal.

**Sacral and Intrasacral Neural Lesions**

Sacral and infrasacral neural lesions interfere with pelvic nerve function resulting in no-reflex micturition and poor bladder storage of urine. Complete sacral injuries result in a denervated pelvic floor and loss of reflex vesical and voiding functions, but leave an intact fixed internal sphincter mechanism. However, complete loss of external sphincter activity is relatively unusual; more frequently, although reflex vesical activity is lost, some pelvic floor activity is retained. Retention of pelvic floor and skeletal muscle activity and perhaps intrinsic external sphincter activity increases urethral outlet resistance, and this in turn increases the bladder pressure required to drive urine across the...
sphincter mechanism. The decentralized bladder shows a positive response to Urecholine (bethanechol chloride) administration, but it also shows a decrease in pressure after administration of anticholinergic agents. Improved vesical tolerance to filling with maintenance of low bladder pressures can be achieved by anticholinergic agents. If not, augmentation cystoplasty may be required to achieve adequate reservoir function and permit management by intermittent catheterization.

Myelodysplasia

Despite controversy in the urological literature, myelodysplasia is associated with a nearly unique type of dysfunction of the bladder and urethra. Typically, the bladder is decentralized and areflexic, and shows poor volume tolerance. The internal or smooth sphincter is not functional, but some external sphincter activity is preserved. Identical findings occur in adults following radical pelvic surgery with injury to both the pelvic nerves and peripheral sympathetic nerves, but not to the pudendal nerve. Incontinence in myelodysplastic patients is due to the loss of internal sphincter function. Paradoxically, 38% of children with this disorder, despite severe incontinence, will with time develop upper tract deterioration. This is directly related to intravesical pressures greater than 40 cm H₂O at the time of urethral urinary leakage. Cystometrograms should be obtained frequently to demonstrate that the bladder pressure is less than 40 cm H₂O. The use of intermittent catheterization and anticholinergic agents reduces the rate of upper tract deterioration to 10% to 15%. When this occurs, it is directly related to intravesical pressures greater than 40 cm H₂O. In cases where the bladder pressure response cannot be controlled, an augmentation cystoplasty to achieve volume tolerance or a surgical reduction in outlet resistance should be performed.²⁸

Intervertebral Disc Herniation and Lower Urinary Tract Dysfunction

Difficulty with the initiation of micturition is common in patients with intervertebral disc disease. This usually is not accompanied by the changes associated with direct neural injury. Changes associated with direct injury to the pelvic nerve are apparent within a few days of the time of the injury. These include a steeper bladder pressure-volume curve than normal, a positive bladder response to administration of Urecholine, and unique waveform activity responses to rapid cystometry, as well as a lack of the external sphincter-guarding reflex response to bladder filling.²⁰,³¹,³⁸ Most patients with intervertebral disc disease show delayed appreciation of the degree of bladder filling and experience difficulty with volitional relaxation of the external sphincter, which is necessary to initiate reflex micturition. These findings, however, are nonspecific and can be induced by electrical stimulation of the pelvic floor or the posterior tibial nerve or by a compression fracture of a vertebral body. Thus, they are not necessarily an indication for immediate operation to preserve vesical function. The depression in normal reflex lower urinary tract function usually requires treatment by catheterization or intermittent catheterization on a temporary basis. Repeated bladder overdistention, even for a short period, can be followed by permanent, apparently local, neural injury to the bladder, with resulting difficulties in voiding and storage function leading to incontinence and residual urine on a permanent basis.

Neurosurgical Intervention and Electrical Stimulation

Surgical interruption of the sacral reflex pathway for micturition may be required in some patients with multiple sclerosis or spinal cord injury, and can be useful in patients with idiopathic detrusor hyperreflexia leading to incontinence. Partial or selective rhizotomy is not effective in the long term, and complete S1-4 intradural sacral rhizotomy (which is permanent) carries with it the problem of poor bladder storage function associated with autonomous responses to bladder filling. In quadriplegics, S2–3 dorsal root ganglionectomy has been reported to induce permanent high-compliance detrusor areflexia and seems to be a more effective method than complete sacral rhizotomy.²⁹

Experimental studies on sacral root stimulation to induce reflex vesical activity show that, although feasible, unwanted contractility of the external sphincter also occurs, which makes “voiding” inefficient.⁴,³⁹,⁴₀ There are three principal methods to circumvent this, including sectioning the branches of the root stimulated that supply the pudendal nerve or arranging high-frequency electrical prestimulation to fatigue the skeletal sphincter, followed by slower-rate stimulation to excite bladder contractility. In addition, since the skeletal sphincter contracts and relaxes rapidly whereas the bladder contracts in a slower, more sustained way, “voiding” during slow-wave stimulation can be induced between sphincter contractions.⁴¹ It is also possible to inhibit reflex detrusor contractility by stimulating the pelvic floor, the anal sphincter, the posterior tibial nerve, or the sacral roots.²⁶

References
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