INTEGRAL STORAGE AND VOIDING REFLEXES

Neurophysiologic Concept of Continence and Micturition

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ABSTRACT — It is a common clinical misconception to regard the spinal micturition reflex center as fundamentally overactive and dependent on cerebral inhibition. Initiation and cessation of micturition is simplistically viewed as a manifestation of voluntary withdrawal and resumption of inhibitory corticospinal "regulation." This view is in conflict with basic neurophysiologic experimental data. Actually, the organization of the micturition reflex is extremely complex. It is affected by multiple sources of facilitative and inhibitory influence, peripheral as well as central. During the past half century, at least twelve reflexes involved in urine storage and coordinated micturition have been described by various neurologic investigators. In this article the integral reflexes are identified and described. A functional organization of the integral reflexes which includes a modern concept of their role in the physiology of urine storage and micturition is presented. It is implicit that overactivity or functional failure of any one or combination of the integral reflexes may cause a significant disorder of lower urinary tract function.

In 1933, in the course of their classic article on the physiology of micturition, Denny-Brown and Robertson1 postulated that the sacral micturition reflex center might be fundamentally overactive and require the constant modulating influence of inhibiting "corticoregulatory tracts." McLellan2 and later Lapides3 and others4 accepted their speculative postulate. According to this simplistic theory, micturition is normally initiated by voluntarily withholding cortical inhibitory impulses to the detrusor reflex and ended by allowing "normal cortical inhibition" to resume at the conclusion of bladder emptying. It is now a common clinical misconception that a defect or developmental delay of corticospinal "regulatory tracts" is a frequent cause of various common urologic conditions, from simple nocturnal enuresis to urgency incontinence and recurrent urinary tract infections.5-11 Based on this obsolescent view of micturition physiology, many urologists make the diagnosis of "uninhibited neurogenic bladder" on the basis of an abnormal cystometrogram in spite of otherwise normal neurologic findings.3,4 Inasmuch as the relative incidence of pathology of inhibitory pathways from the cerebral cortex is greatly exaggerated and other clinically more common sources of abnormal neural influence on the micturition reflex are ignored, this popular clinical interpretation of neurourologic pathology is essentially incorrect. That long tract central nervous system pathology could commonly occur in the spinal cord or in suprapontine pathways causing serious detrusor malfunction, and yet so rarely affect other neurologic functions of the second to fourth sacral segments strains credibility.12 Moreover, there is no evidence of the existence of inhibitory corticospinal tracts affecting the sacral micturition reflex center. The studies of Lewin, Dillard, and Porter13 demonstrated cerebral inhibitory pathways from the
cortex which are extrapyramidal, with multiple interconnections at way stations along the neural axis, probably impacting primarily on the pontine micturition reflex center. These corticopontine pathways do register an important tonic inhibitory influence on the micturition reflex, but there is no evidence that they represent a common site of pathology in otherwise healthy persons. Although Lapides\(^3\) believes that inhibitory as well as facilitative fibers are present in the corticospinal tracts, there is no evidence to substantiate this concept. Nathan and Smith,\(^4\) in their choridotomy studies, found that transection of the micturition pathways in the lateral columns abolished the micturition reflex, but they found no evidence of inhibitory pathways in this area. The only descending fibers in the spinal cord recognized as being inhibitory to the sacral micturition reflex center were identified by Kuru, Koyama, and Kurati\(^5\) and are located in the ventral reticulospinal tracts. They originate in a nucleus in the medulla and represent the centrifugal pathways of the perineobulbar detrusor inhibitory reflex, an important mediator of voluntary cessation of micturition.

Finally, there is abundant evidence that the predominant effect of the brain on the sacral micturition reflex center is one of facilitation, not inhibition, hence the occurrence of total micturition areflexia (spinal shock) following experimental or traumatic suprasacral spinal cord transection.\(^6,7\)

Actually, the organization of the micturition reflex is extremely complex. Its activity, or overactivity, reflects the sum of all inhibitory and facilitative neural influences which act on the pontine and sacral reflex centers. Depending on a great many neural factors, the sacral micturition reflex center may be underfacilitated and voiding may be difficult or impossible to initiate; it may be stable, well-balanced, and function normally; or it may be overfacilitated and unstable, and urgency urinary incontinence may be a symptomatic problem. Tang and Ruch\(^8\) have wisely suggested that the uninhibited neurogenic bladder might be more accurately termed an "overfacilitated neurogenic bladder." This concept of "overfacilitation" has more than semantic importance. It allows for the possibility that abnormal facilitating nerve impulses causing a chronically unstable micturition reflex may have their origin peripherally in nociceptive pelvic afferents and not necessarily in the central nervous system.

There are at least twelve integral pelvic reflexes which are critically important to the normal function of the lower urinary tract. The afferent limbs of these reflexes impact on the pontine or sacral micturition reflex centers or sacral striated sphincter reflex center. Our longstanding clinical infatuation with the naive concept of a so-called "uninhibited neurogenic bladder" has obscured the real importance of these reflexes. The ability to initiate micturition voluntarily, to maintain a strong detrusor contraction to the point of complete bladder emptying, to void at normal pressures and flow rates, to interrupt the urinary stream during micturition, and to avoid the involuntary onset of micturition with increasing detrusor tension or when the pelvic floor is stressed, are all critically dependent on normal function of the integral pelvic reflexes as well as multiple cerebral factors.

The purpose of this article is to present an accurate modern concept of the neurophysiology of the lower urinary tract. After an extensive review of the neurologic literature, we have prepared a functional organization and description of the little known but critically important pelvic reflexes which stabilize and integrate the continence and micturition mechanisms. It is implicit that pathology of the integral reflexes may lead to significant symptomatic disturbances in lower urinary tract function. Neurophysiologic completeness is not possible in an article of this length nor is it intended. Rather, an overview of neurologic factors which appear to be particularly important clinically is presented.

Integral Pelvic Reflexes

Several important reflexes operating between the detrusor and urethra, and the reflex centers in the brain stem and spinal cord have been identified and are listed in Table I. The first four reflexes are concerned with urine storage. The first two are activated by detrusor stretch receptors and increase in activity as bladder volume and detrusor mural tension increase.\(^8\) The first, the sympathetic detrusor-inhibiting reflex (SDIR), results in inhibition of detrusor contractility. The second, the sympathetic sphincter-constrictor reflex (SSCR), produces increasing internal sphincter tone. Together they comprise the "sympathetic stabilizing reflexes" favoring continence of urine. The afferents pass over the pelvic nerves and the
<table>
<thead>
<tr>
<th>Reflex Number</th>
<th>Name and Abbreviation</th>
<th>Activating Stimulus</th>
<th>Afferent Route</th>
<th>Efferent Route</th>
<th>Location of Reflex Center</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sympathetic detrusor-inhibiting reflex (SDIR)</td>
<td>Increasing detrusor mural tension</td>
<td>Pelvic nerves</td>
<td>Hypogastric nerves</td>
<td>Thoracolumbar cord</td>
<td>Storage of urine</td>
</tr>
<tr>
<td>2</td>
<td>Sympathetic sphincter constrictor reflex (SSCR)</td>
<td>Increasing detrusor mural tension</td>
<td>Pelvic nerves</td>
<td>Hypogastric nerves</td>
<td>Thoracolumbar cord</td>
<td>(Reflex 12, in tonic phase also serves storage function)</td>
</tr>
<tr>
<td>3</td>
<td>Perineodetrusor inhibitory reflex (PDIR)</td>
<td>Tension of perineal and pelvic floor muscles</td>
<td>Pudendal nerves</td>
<td>Pelvic nerves</td>
<td>SMRC (sacral cord)</td>
<td>Initiation of micturition</td>
</tr>
<tr>
<td>4</td>
<td>Urethrosphincteric guarding reflex (USGR)</td>
<td>Tension of trigone or entry of urine into proximal urethra</td>
<td>Pudendal nerves</td>
<td>Pudendal nerves</td>
<td>Pudendal nucleus (sacral cord)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Perineobulbar detrusor facilitative reflex (PBDFR)</td>
<td>Relaxation of perineal and pelvic muscles associated with increase in intra-abdominal pressure</td>
<td>Pudendal nerves; sacrobulbar tracts</td>
<td>Lateral reticulospinal tracts and pelvic nerves</td>
<td>Medulla to SMRC (sacral cord)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Detrusodetrusor facilitative reflex (DDFR)</td>
<td>Increasing detrusor mural tension</td>
<td>Pelvic nerves and dorsal funiculus</td>
<td>Lateral reticulospinal tracts and pelvic nerves</td>
<td>Rostral pons to SMRC (sacral cord)</td>
<td>(Reflexes 9 and 10 may also be initiating reflexes)</td>
</tr>
<tr>
<td>7</td>
<td>Destrusourethral inhibitory reflex (DUIR)</td>
<td>Increasing detrusor mural tension</td>
<td>Pelvic nerves</td>
<td>Pelvic nerves</td>
<td>SMRC (sacral cord)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Destrusosphincteric inhibitory reflex (DSIR)</td>
<td>Increasing detrusor mural tension</td>
<td>Pelvic nerves</td>
<td>Pudendal nerves</td>
<td>Pudendal nucleus (sacral cord)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Urethrodetrusor facilitative reflex (UDFR)</td>
<td>Urine flow across urethral mucosa</td>
<td>Pudendal nerves and lateral funiculus</td>
<td>Lateral reticulospinal tracts and pelvic nerves</td>
<td>Rostral pons to SMRC (sacral cord)</td>
<td>Continuation of detrusor contraction to empty bladder and synchronization of sphincter relaxation</td>
</tr>
<tr>
<td>10</td>
<td>Urethrodetrusor facilitative reflex (UDFR)</td>
<td>Urine flow across urethral mucosa</td>
<td>Pelvic nerves</td>
<td>Pelvic nerves</td>
<td>SMRC (sacral cord)</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Urethrosphincteric inhibitory reflex (USIR)</td>
<td>Urine flow across urethral mucosa</td>
<td>Pudendal nerves</td>
<td>Pudendal nerves</td>
<td>Pudendal nucleus (sacral cord)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Perineobulbar detrusor inhibitory reflex (PBDIR)</td>
<td>Contraction of perineal and pelvic muscles</td>
<td>Pudendal nerves and sacrobulbar tracts</td>
<td>Ventral reticulospinal tracts</td>
<td>Medulla to SMRC (sacral cord)</td>
<td>Cessation of voiding and resumption of storage phase</td>
</tr>
</tbody>
</table>
efferent pathways are via the hypogastric nerves. The third reflex, the perineodetrusor inhibitory reflex (PDIR), is activated by tension receptors in the striated muscle of the perineum and pelvic floor, particularly the puboococygeus.\textsuperscript{1,18,20} Resting muscle tone causes a tonic inhibitory influence on the sacral micturition reflex center (SMRC) which may be increased with higher levels of voluntary contractions. The afferent pathway is over the pudendal nerves and posterior roots of the third and fourth sacral segments. The fourth reflex, the urethrosphincteric guarding reflex (USGR), is activated by increased mural tension in the trigone and bladder neck as bladder filling progresses or by escape of urine into the proximal urethra.\textsuperscript{21} Activation of the reflex results in an increase in tone of the striated external sphincter. Both afferent and efferent pathways are over the pudendal nerves. This reflex is inhibited by integral reflex 6 and possibly by integral reflex 5 as well. Coordinated voiding is therefore dependent on the integrity of ascending and descending spinal cord pathways. In its tonic phase reflex 12, to be described later, also sub-
serves the storage function.\textsuperscript{15}

The fifth and sixth reflexes are concerned with the initiation of micturition. The fifth reflex, the perineoebulbar detrusor facilitative reflex (PBDFR), is activated by voluntary contraction of the diaphragm and abdominal wall muscles and simultaneous relaxation of the pelvic floor and perineal muscles.\textsuperscript{29} Afferent impulses from perineal muscle stretch receptors ascend in the sacrocolubran tracts facilitating the vesicoconstrictor center in the medulla. The vesicoconstrictor center inhibits the bulbar vesicorelaxor center and facilitates the SMRC over pathways in the lateral reticulo spinal tract. These pathways constitute an important reflex mechanism for the voluntary initiation of micturition. The sixth through the eighth reflexes are activated by stretch receptors located in the detrusor muscle and are stimulated by increasing mural tension as the bladder fills. The sixth reflex, the detrusodetrusor facilitative reflex (DDFR), long routes via pelvic nerve afferents and ascending fibers in the anterolateral funiculus of the spinal cord to the pontine micturition reflex center (PMRC) where it is strongly facilitative.\textsuperscript{23,24} The PMRC in turn facilitates the sacral micturition reflex center (SMRC) over fibers which contribute to the lateral reticulo spinal tracts.\textsuperscript{25} For many individuals, the facilitative influence of the sixth reflex is an important prerequisite for voluntary initiation of micturition. Reflexes 9 and 10, to be described later, may also function in initiating micturition and in some may represent the primary initiating facilitative mechanism.\textsuperscript{29}

The seventh through eleventh reflexes are concerned with maintaining a strong detrusor contraction throughout the voiding phase to provide for complete emptying of the bladder and for synchronous relaxation of the sphincters during the voiding phase. The seventh reflex, the detrusourethral inhibitory reflex (DUIR), results in inhibitory motor impulses to the bladder neck and proximal urethra, the functional smooth muscle zone to which the term "internal sphincter" is commonly applied. The afferents and efferents are located in the pelvic nerves and the reflex center is the SMRC. The eighth reflex, the detrusosphincteric inhibitory reflex (DSIR), sends inhibitory impulses via the pelvic nerves to the "pudendal nucleus," the sacral striated sphincter reflex center in the anterior horn of the third and fourth sacral level.\textsuperscript{23} The ninth through eleventh reflexes originate in the urethra and are activated by urine entering the proximal urethra stimulating neuroreceptors sensitive to the flow friction or to an increase in urethral static pressure in this zone. The ninth and tenth reflexes are the urethrodetrusor facilitative reflexes (UDFR), the afferents of which increase the excitability of the micturition reflex.\textsuperscript{23,27} The ninth reflex consists of afferent fibers which pass via the pudendal nerves and long route to the PMRC over ascending fibers in the posterior columns.\textsuperscript{28} Increased SMRC excitation results from increased facilitative impulses over descending fibers in the lateral reticulo spinal tracts. The afferents of the tenth reflex pass via the pelvic nerves directly to the SMRC.\textsuperscript{23} Both reflexes are facilitative to the micturition reflex, but the ninth is the more powerful of the two. The efferents are, of course, the motor neurons from the SMRC to the detrusor in the pelvic nerves. The eleventh reflex, the urethrosphincteric inhibitory reflex (USIR), has both afferents and efferents in the pudendal nerves.\textsuperscript{23} It is responsible for the prompt synchronous relaxation of the external sphincter at onset of micturition and is additive to the effect of the eighth reflex (DSIR) in this regard.

The twelfth reflex, the perineobulbar detrusor inhibitory reflex (PBDIR), is in large part responsible for the suppression or voluntary cessation of micturition.\textsuperscript{15} It is activated by
voluntary contraction of the pelvic floor and perineal muscles, particularly the pubococcygeus muscles. Afferent fibers from the stretch receptors of these muscles pass over the pudendal nerves and impact, in part, directly on the pudendal nucleus (third reflex) and in part ascend in the sacrobulbar tracts to the brain stem where they act to inhibit the bulbar vesicocentstor center and excite the bulbar vesicorelaxer center. The vesicorelaxer center sends inhibitory impulses to the SMRC over fibers in the ventral reticulospinal tract, suppressing SMRC excitability to a resting level and providing for the reestablishment of the activity of the storage reflexes (reflexes 1 through 4) as micturition is concluded.

Micturition Reflex

When the summation of all facilitative impulses reaching the SMRC from cerebral and peripheral sources exceeds the summation of inhibitory influence by a sufficient margin that threshold excitability is reached, a motor discharge to the detrusor occurs. Detrusor motor innervation is delivered via the pelvic nerves over neurons which originate in the intermediolateral columns of the spinal cord between the second and fourth sacral segments, primarily in the third and fourth, in clusters of cells which make up the SMRC (Fig. 1).\(^{29-35}\) The motor neurons terminate in synapses with ganglion cells in the vesical plexus and the detrusor muscle fibers are innervated by short, postganglionic fibers. Except for minor fluctuations of detrusor tone, an intrinsic function of the smooth muscle, the detrusor contracts only when it is stimulated by a motor discharge from the SMRC. When the bladder is “stable,” even the highly facilitative state of bladder fullness is subthreshold, and the SMRC does not reach a critical excitation level. Accordingly, a detrusor contraction does not occur unless and until voluntary facilitation is added. When the micturition reflex is facilitated to a supra-threshold level without voluntary facilitation, voluntary inhibition is required to avoid motor stimulation of the detrusor and the bladder is said to be “unstable.”

Transsection, stimulation, and ablation studies show that the micturition reflex center is influenced by a number of cerebral areas above the pons. The cortex is capable of both inhibition and facilitation.\(^{36-38}\) In the limbic system there are areas producing both facilitative and inhibitory influence, and it is in this area that the autonomic and somatic nervous systems have some common origin.\(^{39}\) Areas in the hypothalamus are predominantly facilitative to the micturition reflex.\(^{40,41}\) In the midbrain, at the level of the superior colliculus, there is an inhibitory area.\(^{40,41}\) Both facilitative and inhibitory areas have been demonstrated in the cerebellum. But the net cerebella effect is one of inhibition.\(^{42}\) In the rostral pons there is an important micturition reflex center (PMRC) which exerts tonic facilitative influence on the SMRC over fibers which descend in the lateral reticulospinal tract.\(^{43,44}\)

Using stereotactic and Marchi techniques, Kuru and his co-workers have identified bulbar-sacral pathways associated with facilitative and inhibitory vesicomotor centers in the proximal medulla.\(^{15,22,25}\) Centrifugal facilitative fibers descend from a nucleus in the lateral reticular formation over the lateral reticulospinal tracts, facilitating the SMRC. Neurons inhibitory to the SMRC originate in the vesicorelaxer center in the medial reticular formation and descend through the ventral reticulospinal tracts. Both
FIGURE 2. Facilitative influence on micturition reflex. Integral voiding reflexes: reflex 5 is activated by voluntary relaxation of pelvic floor and perineal muscles; reflexes 6, 7, and 8 are activated by stretch receptors in detrusor muscle; reflexes 9, 10, and 11 are activated by mucosal receptors in proximal urethral sensitive to urine flow or increased urethral static pressure (Table 1).

Facilitative Influence on SMRC

The activity of the SMRC is dependent on the balance of all the neural factors which affect it directly and which modulate the level of facilitative excitability of the pontine micturition reflex center. There are six major facilitative and three major inhibitory neural influences on the SMRC. First, the net effect of all cerebral influences on the SMRC is facilitative and the SMRC is dependent on this strong basal facilitation from the PMRC (Fig. 2). To this tonic basal level further facilitation of the SMRC may be voluntarily initiated in two ways.

First, voluntary relaxation of the pelvic floor muscles has an indirectly facilitative influence on the SMRC. This occurs, in part, from decreased excitation of the muscle stretch receptors which normally produce some tonic basal level of inhibition directly upon the SMRC (reflex 3).

Second, there is some evidence suggesting that facilitation of the SMRC may also be voluntarily produced even during curare-induced striated muscle paralysis. Whether this influence may be exerted by direct cortical pathways to the PMRC or simply by cortical impulses acting on the next lower subcortical way station in the neural axis or perhaps even by voluntary diminution of sympathetic influence is not known.

Another important facilitative influence is the afferent limb of the detrusodetrusor facilitative reflex. As the bladder fills and detrusor mural tension increases, stretch receptors in the detrusor muscle are increasingly activated and send facilitative afferent impulses to the PMRC over the pelvic nerves and ascending pathways in the spinthalamic tracts. The same receptor unit is excited by both passive distention and by active contraction and these two sources of impulses can summate. The sensory receptors vary through a wide spectrum of sensitivity. As mural tension increases with a detrusor contraction, more and more stretch receptors are activated. The reflex is, in effect, an automultiplier and is important in facilitating the initiation of voiding, normally raising the level of excitability in the SMRC to a point where threshold level is easily achievable by additional voluntary facilitation. However, during the midvoiding phase, as bladder emptying progresses, detrusor mural tension may wane and additional facilitation to the SMRC from another source is necessary if suprathreshold excitation is to be maintained. Strong facilitation helpful in producing continuing contraction of the detrusor to complete emptying is provided by integral reflexes 9 and 10, the urethrodetrusor facilitative reflexes (Fig. 2).

Inhibitory Influence on SMRC

In addition to the multiple cerebral sources of tonic inhibitory influence acting on the PMRC, voluntarily variable inhibitory influence on the micturition reflex appears to have at least three
Figure 3. Inhibitory influence on micturition reflex. Integral storage reflexes: reflexes 1 and 2, sympathetic stabilizing reflexes, are activated by detrusor stretch receptors sensitive to increasing mural tension. Reflex 3, perineodetrusor inhibitory reflex, is activated by stretch receptors in pelvic floor and perineal muscles. Reflex 4, urethrosphinicteric guarding reflex, is activated by increasing mural tension in trigone and bladder neck as bladder filling progresses (Table 1).

sources (Fig. 3). One important tonic inhibitory influence is from the afferent limb of the perineodetrusor inhibitory reflex (reflex 3). The afferent impulses originate in the stretch receptors in the striated muscles of the pelvic floor and perineum, especially the pubococcygeus. These fibers reach the spinal cord over the pudendal nerves and the dorsal roots of third and fourth sacral segments. Other fibers (reflex 12) ascend in the sacroccocygeal tract and excite the vesicorelaxer center in the medulla. This center sends inhibitory impulses to the SMRC over fibers in the ventral reticulospinal tracts. The tone of the pelvic floor muscles provides an important basal level of tonic inhibitory influence on the SMRC. The effect of the guarding reflex (reflex 4) is to augment the activity of reflexes 3 and 12 automatically as bladder filling progresses and as mural tension in the trigone and bladder neck increases. When the bladder is stable, this inhibitory effect is sufficient to counteract or suppress all involuntary facilitative influence on the SMRC. Voluntary contraction of the pelvic floor and perineal muscles, and external sphincter mediated by corticospinal pyramidal pathways causes additional activation of the muscle stretch receptors. This results in a much higher level of SMRC inhibition and during micturition, when the bladder is stable, produces complete relaxation of the detrusor after a brief latency period. Accordingly, the stable bladder may be voluntarily inhibited even during midvoiding, not only by striated sphincteric occlusion of the urethral lumen, voluntarily overriding reflexes 8 and 11, but also by simultaneous reflex inhibition of the detrusor contraction (reflexes 3 and 12), overriding the facilitative influence of the detrusodetrusor and urethrodetrusor reflexes (reflexes 6, 9, and 10).

Another voluntary inhibitory pathway exists, the action of which is less prompt but sufficiently strong to interrupt and suppress a detrusor contraction during the midvoiding phase. Lapidides, Sweet and Lewis have shown that even during curare-induced striated muscle paralysis, micturition could be voluntarily interrupted, although a ten- to twelve-second period was required to effect complete cessation or urinary flow. The pathway of this inhibitory effect remains uncertain. There is no evidence for the existence of long "corticospinal inhibitory tracts" in the pyramidal system as Lapidides and co-workers have suggested. The cortically initiated voluntary inhibition is probably carried over multiple short pathways and way stations acting ultimately on the PMRC.

The possibility exists that a voluntarily achieved increase in the motor activity of the sympathetic innervation of the detrusor and internal sphincter may be involved. The possibility of this latter inhibitory route is suggested by Miller's interesting investigation of voluntary autonomic control. This voluntary inhibitory influence, whatever its pathways, is probably the first-line mechanism of voluntary inhibition, called into play in mild instability states whenever bladder filling produces threshold or near-threshold excitability of the SMRC.

The sympathetic nervous system is not essential to micturition but does represent an important stabilizing influence on the micturition reflex by inhibiting the detrusor (reflex 1) and by increasing the tone of the internal sphincter (reflex 2). This effect enhances the capacity of the bladder to store a larger volume without involuntary escape of urine. Detrusor stretch receptors activate these reflexes. The afferent fibers pass to the spinal cord in the
pelvic nerves and upward in the cord to a thoracolumbar sympathetic reflex center located between the eleventh thoracic and fourth lumbar vertebrae. Efferent impulses originating in this center pass in preganglionic fibers to the paravertebral ganglia and over postganglionic fibers in the hypogastric nerves to the detrusor and to the internal sphincter. Many of these postganglionic fibers terminate in the "parasympathetic" pelvic ganglia.\textsuperscript{56,57} Sympathetic motor innervation has a net beta or relaxer effect on the detrusor, increasing the bladder volume at which the micturition reflex is triggered in experimental animals.\textsuperscript{55} The inhibition of detrusor contractility may be effected, in part, at the pelvic ganglionic level where there is a rich anatomic interconnection of pre- ganglionic cells. Conversely, sympathetic innervation has a net alpha or constrictor effect on the trigone, intramural ureteral musculature, bladder neck, and proximal urethra. The normal action of the sympathetic nervous system is to augment continence by providing a constant detrusor-sphincter stabilizing effect with a built-in multiplying feedback mechanism which increases sympathetic motor activity as bladder filling progresses and as detrusor mural tension increases (Fig. 2).\textsuperscript{18} Cessation of sympathetic influence on the detrusor and internal sphincter occurs synchronously with activation of the micturition reflex.\textsuperscript{68} Whether this is accomplished by direct inhibition of the thoracolumbar center, by ascending pathways from the SMRC (Fig. 2), or by descending pathways from the bulbous vesicoconstrictor center is not known. In some patients with spinal cord lesions ineffective micturition associated with asynchronous persistence of sympathetic innervation and inappropriately high internal sphincter tone, more effective voiding can be restored by alpha-adrenergic blockade with a blocking agent such as phenoxybenzamine.\textsuperscript{59}

Imipramine often produces temporary symptomatic improvement in the management of urinary incontinence by sensitizing the alpha adrenergic neurorceptors of the internal sphincter, and the beta detrusor receptors, thus augmenting the sympathetic detrusor/sphincter stabilizing effect of reflexes 1 and 2.\textsuperscript{60} There is evidence suggesting that congenital deficiency in the density or distribution of alpha-adrenergic receptors in the region of the internal sphincter may be a significant underlying etiologic factor in some cases of juvenile urinary incontinence.\textsuperscript{61}

Physiology of Voluntary Micturition

Initiation of micturition in the normal individual represents a complex series of events. It is possible that the order and importance of events may vary, to some extent, from person to person and even in the same individual from time to time depending, for example, on the degree of bladder fullness when initiation of micturition is attempted.

It is generally agreed that the increased mural tension of bladder fullness is an important facilitative stimulus for voluntary onset of micturition. Most investigators also agree that the initial event in voluntary micturition is the relative fixation of abdominal muscles and diaphragm associated simultaneously with gentle increase in intra-abdominal pressure and voluntary relaxation of the pelvic floor and perineal muscles.\textsuperscript{1,4,62} This results in descent of the pelvic floor and bladder base and a decrease in urethral closure pressure.\textsuperscript{63,64} Opening of the bladder neck is usually not fluoroscopically demonstrable simultaneous with the descent, but it usually follows a few seconds later after onset of detrusor contraction. Decrease in the extrinsic muscular support and shortening of the urethra with descent enhances "dilatability" of internal sphincter as detrusor contraction begins.

More important, however, are the reflex mechanisms which lead to detrusor contraction and internal sphincter relaxation. Fixation of the diaphragm and rectus muscles and relaxation of the pubococcygeus muscle facilitate the SMRC by mechanisms described previously (reflexes 3 and 5). The voluntary relaxation of the perineum is usually followed within a few seconds by a motor discharge from the SMRC causing an active detrusor contraction.\textsuperscript{65} This is associated with simultaneous inhibition of the sympathetic detrusor-sphincteric reflexes (reflexes 1 and 2) resulting in decreased internal sphincter tone.\textsuperscript{58} Increasing mural tension associated with the detrusor contraction further activates the detrusor-detrusor reflex, a multiplication reflex, exciting the PMRC which further augments the suprathreshold excitability of the SMRC resulting in a detrusor contraction of increasing force. Reflex 4, the guarding reflex, is inhibited and inactivated by reflex 6.

Karlson\textsuperscript{68} has shown that in some individuals the entry of a small quantity of urine into the proximal urethra after the initial drop in closure pressure may be the critical stimulus which elicits a detrusor contraction (reflexes 9 and 10).
This suggests that reflex 5 as well as reflex 6 may inhibit and inactivate the guarding reflex (reflex 4). With increasing detrusor mural tension the DSI reflex is activated, inhibiting the sacral external sphincter center (pubendal nucleus) producing relaxation of the external sphincter. Inhibition of striated sphincter tone may sometimes precede a detrusor contraction, an effect which may be part of the perineobulbar detrusor facilitative reflex mediated via the bulbar vesicomotor centers with inhibitory fibers to a pontine striated sphincter facilitative center.44

As parasympathetic discharge from the SMRC increases, direct inhibition of the bladder neck and proximal urethral tonus is produced. There is recent evidence suggesting that this inhibitory effect is mediated at the ganglionic level by interaction with postganglionic adrenergic fibers.55 With increasing detrusor mural tension the bladder neck abruptly opens. Whether bladder neck opening is primarily a neurologically mediated event or a mechanical event resulting from the particular orientation of muscular and elastic tissues at the base of the bladder, remains a controversial point. In recent years there has been some popularization of mechanistic views that the "base plate" is broken56 or that the bladder neck is simply "pulled open" during detrusor contraction67 by action of the longitudinally oriented fibers of the detrusor inserting in the urethra.

This mechanical concept of bladder neck opening was originally conceived by Kohlrausch in 1864 and given impetus by the anatomic studies of Wesson68 and Woodburne,69 and has been supported in recent years by Lapides,67 and Hutch66 and Tanagho and Smith.70 However, the weight of evidence persuades against this popular view. On the basis of embryologic studies, Droes71 disagrees with Woodburne's69 view that the detrusor and internal sphincter are anatomically continuous and believe that they develop as entirely separate muscular structures. The simultaneous electromyographic studies of detrusor and internal sphincter by Franksson and Petersen,72 the neurophysiologic studies of Gerado and Campbell,59 and Bradley and Teague,56 the microanatomic studies of Gosling and Dixon,73 and studies by numerous other investigators,35,34,51,53,54 provide compelling evidence for a neurologically mediated reciprocal control of detrusor and internal sphincter. Furthermore, the recent histologic demonstration of rich sympathetic and parasympathetic interconnections at the pelvic ganglionic level,58,57 and the pharmacologic studies of Kleeman,74 Raz and Caine,75 Krane and Olsson,76 and Nergardh60 lend additional support to the view that neurologic factors play a major role in integrating normal synchronous function of the detrusor and internal sphincter.

As the bladder neck opens, the proximal urethra is exposed to urine flow and to a sudden increase in intraluminal static pressure. The UDF reflexes are activated, further increasing the PMRC and SMRC excitability and facilitating the detrusor contraction to complete bladder emptying. With onset of urine flow and increased pressure in the proximal urethra, the USI reflex (reflex 11) is also activated, adding to the prior influence of the DSI reflex, effecting continuous relaxation of the external sphincter until the completion of micturition. The guarding reflex (reflex 4), having been inhibited by the previously activated reflex 6, remains inoperative. Any spinal cord injury or disease interfering with the ascending pathways of reflex 6 in the anterolateral funiculus may interfere with synchronous inhibition of the guarding reflex at the onset of micturition. Failure of this critical integration mediated via the brain stem would result in detrusor-sphincter dysynergy. In the absence of normal suppression of the guarding reflex, alternating excitation of reflex 8 and reflex 4 may result in intermittent spurts of urine flow repeatedly interrupted by clonic dysynergic sphincter contractions.

Micturition, thus voluntarily initiated and automatically synchronized by the integral reflexes, may proceed to completion at normal intravesical and intrarethral pressures and normal flow rates, assuming that the outflow tract is anatomically free of hydraulically compromising defects. When the bladder is empty and urinary flow ceases, voluntary contraction of the pelvic floor and perineal muscles elicits reflex 12, the perineobulbar detrusor inhibitory reflex. This causes activation of the bulbar vesicoureilaxer center and the SMRC is inhibited. Motor impulses over the pelvic nerve cease, detrusor mural tension returns to resting level, and parasympathetic inhibition of the internal sphincter ceases. Inhibition of the striated sphincter reflex center (pubendal nucleus) is ended and normal basal external sphincter tonus returns. The final stage in the cycle is completed, with resumption of normal activity of the sympathetic stabilizing reflexes, the tonic perineal
inhibitory reflexes, and the guarding reflex, and a new storage or filling phase begins.

"Uninhibited Neurogenic Bladder" in Critique

The clinical concept of "uninhibited neurogenic bladder" as the major cause of detrusor overactivity problems represents a convenient but simplistic view of bladder malfunction. It derives from the erroneous physiologic conception originated by Denny-Brown and Robertson,¹ and popularized by McLellan² and Lapides,³ of a sacral micturition reflex center which is fundamentally overactive and dependent for normal function on corticospinal inhibition. The diagnosis of "uninhibited neurogenic bladder" is frequently assigned by clinicians to patients in whom neurologic deficit is demonstrable, but in whom atropine-suppressible involuntary detrusor contractions are demonstrated by cystometry.³,⁵,⁸,¹¹ The diagnostic concept is simplistic because it overlooks the many facilitative and inhibitory neural influences which act on the SMRC and is frankly erroneous because it views the brain as providing a constant basal inhibiting influence on the SMRC. Actually, the SMRC should be considered as existing in a relatively critical physiologic balance of many facilitative and inhibitory vectors, from peripheral as well as central sources. Over-facilitation from any source may cause the SMRC to discharge prematurely, not only without voluntary facilitation, but even in spite of voluntary inhibition by contraction of the striated sphincter and pelvic floor muscles. Suppression of detrusor hyperreflexia by propantheline (Pro-Banthine) or atropine, which blocks in the final common motor pathway, indicates a neurologic mediation of the involuntary detrusor contractions but provides no evidence as to the source of the overfacilitation. In a subsequent article we will present evidence of a common unstable bladder syndrome in which atropine-suppressible micturition hyperreflexia is caused by overactivity of integral reflexes 9 and 10, caused by surgically correctable primary pathology in the urethra.⁷⁷

There is abundant evidence that the sacral micturition reflex center receives net facilitation from the brain, not inhibition.¹⁶,¹⁷,⁴⁴ One group of investigators avoids inconsistency with this neurophysiologic reality and at the same time retains the clinical concept of "uninhibited neurogenic bladder" by suggesting that the micturition reflex center is located in the brain stem not in the lower spinal cord.⁷⁸ They emphasize its dependence on cerebral inhibition and apparently overlook the clinical and experimental evidence indicating that an important micturition reflex center exists at the sacral level as well. This oversimplification of micturition neurophysiology risks serious clinical misunderstanding and mismanagement.

The phase of spinal shock after spinal cord transection with which clinicians are familiar is a period of peripheral areflexia which results from loss of essential net facilitative influence from cerebral sources. The late return of micturition reflex activity and even of detrusor spasticity states does not reflect loss of cerebral inhibition as some urologists have thought.²,³,⁷⁹ Rather, it reflects the activity of peripheral afferent impulses acting on a pathologic, denervated and, in some cases, hypersensitive sacral micturition reflex center. Our present understanding of denervation hypersensitivity mechanisms is very limited,⁸⁰ but it should not confuse our concept of normal physiology.

In 1971, Bates⁸¹ introduced the term "unstable bladder" to describe the clinical situation characterized by involuntary uninhibitable detrusor contractions during cystometry. This term allows for the neuromuscular complexities of lower urinary tract function and it introduces no erroneous connotations. It should replace the term "uninhibited neurogenic bladder" in common clinical parlance and the latter term should be reserved for those relatively less common bladder instability problems in which examination reveals real evidence of a neurologic lesion involving specific inhibitory pathways.

Vesical Outlet Obstruction and Unstable Bladder

As a consequence of vesical outlet obstruction, or facilitative hyperreflexia, long-standing muscular overwork often leads to hypertrophy of the detrusor. This compensatory detrusor response is particularly characteristic of young children. The hypertrophied detrusor may act as a source of significant overfacilitation of the micturition reflex. It is well established that bladder tonus is an intrinsic myogenic property independent of any tonic influence from the central nervous system.⁸⁵,⁸⁶ However, hypertrophy of the detrusor may lead to a significant increase in bladder tonus. A higher level of resting detrusor tonus may result in an increased
activation of detrusor stretch receptors and cause chronic overfacilitation of the PMRC.46,47

Some urologists have commented on the striking cystometric similarity of certain obstructed bladders to the "uninhibited neurogenic bladder."19,84 Turner-Warwick has noted the reversal of cystometric abnormality following relief of obstruction. Yet, because detrusor hypertrophy does tend to persist after its cause is corrected, any neurologic overfacilitation secondary to hypertrophy may also be of relatively limited reversibility. Therefore, the presence of obstructive or any nociceptive facilitative reflex pathology which may cause detrusor hypertrophy deserves to be recognized and, if possible, corrected early, before a significant overfacilitative state is established.

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