
Normal and Abnormal Function: An Overview

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The bladder (reservoir) and its outlet function as a pair of interrelated structures whose coordinated actions in the adult normally bring about (1) low-pressure reservoir filling and urine storage without involuntary leakage and (2) periodic voluntary emptying of the system, again at low pressure [1, 2]. The neuroanatomic, physiologic, and pharmacologic milieu which normally serves as a background and operating system for this simple sounding cycle is well described in the previous chapter. For conceptualization and a framework for evaluation, categorization, and management of abnormal function, it is logical to consider these two phases as relatively discrete: bladder filling and urine storage, and bladder emptying/voiding [3]. This micturition cycle normally displays these two modes of operation in a simple on-off fashion [4–6] which involves (1) activation of storage reflexes affecting the outlet and inhibiting the detrusor contraction reflex and (2) switching to inhibition of the storage reflexes and concomitant activation of the voiding reflex—and back again. As an easy to understand framework for subsequent discussion of evaluation, categorization, and management, the basics of these two phases are summarized followed by a brief description of what can and does malfunction.

Normal Function [4, 6–9]

The normal adult bladder response to filling at a physiologic rate is an almost imperceptible change in content pressure. During at least the initial stages of bladder filling, this very high compliance (Δ volume/ Δ pressure) is due primarily to the elastic and viscoelastic properties of the bladder wall which allow it to stretch to a certain degree without any increase in tension exerted on its contents. The viscoelastic properties of the stroma (bladder wall less smooth muscle and epithelium) are due to its primary components, collagen and elastin. There may also be an active but non-neurogenic component to the filling/storage properties of the bladder. Some have suggested that an as yet unidentified relaxing factor is released from the urothelium, and others have suggested urothelium released nitric oxide may exert an inhibitory effect on the afferent mechanisms during filling. At physiologic filling rates, intravesical pressure remains essentially unchanged. In the clinical setting, filling cystometry normally shows a slight increase in detrusor pressure, but this pressure rise is a function of the fact that clinic cystometry filling is always carried out at a greater than normal physiologic rate.

At a certain level of bladder filling, spinal sympathetic reflexes are evoked in many animals, and there is evidence to support such a role for at least some components of these in humans. There are three limbs to this sympathetic reflex (see Fig. 2.1).

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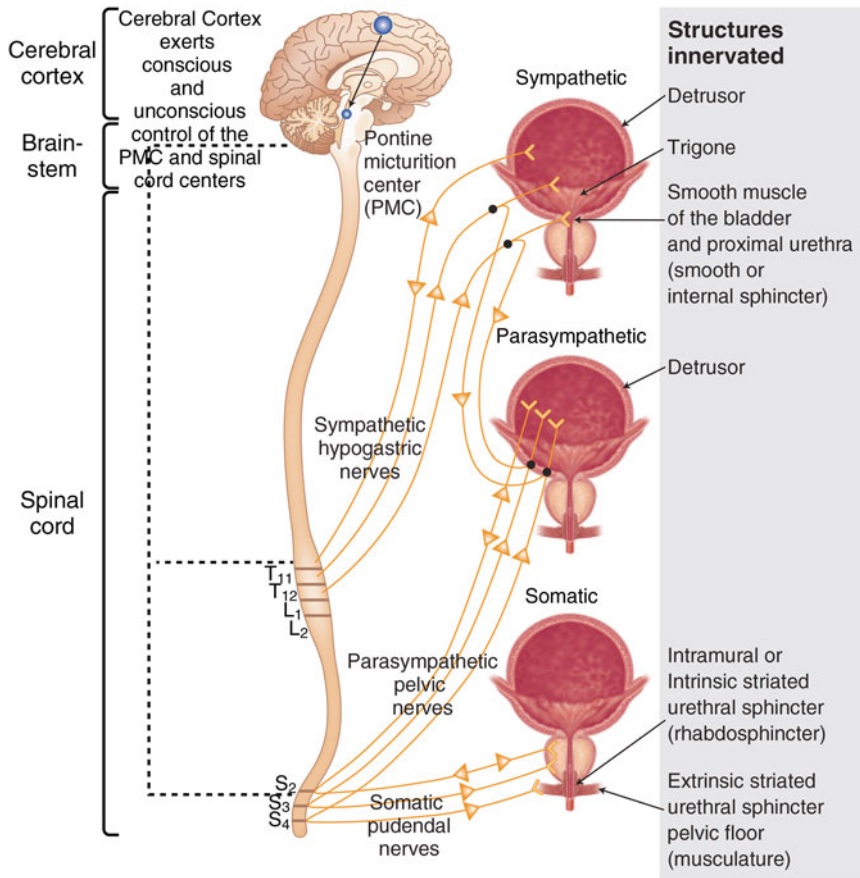


Fig. 2.1 Current conceptualization of lower urinary tract innervation by somatic (pudendal nerve) and autonomic (sympathetic and parasympathetic) nervous systems (modified after Newman and Wein [10]; courtesy of Robin Noel)

One is neurally mediated stimulation of the predominantly α -1a adrenergic receptors in the area of the bladder neck and proximal urethra, the net result of which would be to cause an increase of resistance in that area. One is neurally mediated stimulation of the predominantly β -3 adrenergic receptors in the bladder body smooth musculature, causing a decrease in tension. The third is an inhibitory effect on bladder contractility thought to be mediated primarily by sympathetic modulation of parasympathetic ganglionic transmission. Good evidence seems to also support a strong tonic inhibitory effect of endogenous opioids and other transmitters on bladder activity at the level of the spinal cord, the parasympathetic ganglia, and the brain stem as well. Finally, bladder filling and wall distention may release autocrine-like

factors which themselves influence contractility, either by stimulation or inhibition.

There is a gradual increase in urethral pressure during bladder filling primarily contributed by a striated sphincter reflex. The rise in urethral pressure seen during the filling and storage phase of micturition can be correlated with an increase in efferent pudendal nerve impulse frequency. This constitutes the efferent limb of a spinal somatic reflex that is initiated when a certain critical intravesical pressure is reached, the so-called guarding reflex, which results in an increase in striated sphincter activity.

The passive properties of the urethral wall also undoubtedly play a large role in the maintenance of continence. Urethral wall tension develops within the outer layers of the urethra; however,

it is a product not only of the active characteristics of smooth and striated muscle but also of the passive characteristics of the elastic and collagenous tissues that make up the urethral wall. In addition, this tension must be exerted on a soft, plastic inner layer capable of being compressed to a closed configuration—the “filler material” representing the submucosal portion of the urethra. The softer and more plastic this area is, the less pressure required by the tension-producing layers to produce continence. Finally, whatever the compressive forces, the lumen of the urethra must be capable of being obliterated by a watertight seal. This mucosal seal mechanism explains why a very thin-walled rubber tube requires less pressure to close an open end when the inner layer is coated with a fine layer of grease than when it is not—the latter case being analogous to scarred or atrophic urethral mucosa [11].

Continence during increases in intra-abdominal pressure is maintained by (1) the effects of the spinal somatic and sympathetic reflexes on the striated and smooth sphincter areas, the intrinsic competence of the bladder outlet, and, in the female, urethral compression against a suburethral supporting layer. A further increase in striated sphincter activity on a reflex basis (the cough reflex) is also contributory.

Normally, it is increased detrusor pressure producing the sensation of fullness that is primarily responsible for the initiation of voluntary induced bladder emptying. Although the origin of the parasympathetic neural outflow to the bladder, the pelvic nerve, is in the sacral spinal cord, the actual organizational center for the micturition reflex in an intact neural axis is in the brain stem (pontine-mesencephalic formation), and the complete neural circuit for normal micturition includes the ascending and descending spinal cord pathways to and from this area and the facilitatory and inhibitory influences from other parts of the brain.

The final step in voluntarily induced micturition initially involves inhibition of the reflex responsible for increased somatic neural efferent activity to the striated sphincter and an inhibition of all aspects of any spinal sympathetic reflexes evoked during filling. Efferent parasympathetic

pelvic nerve activity is ultimately what is responsible for a highly coordinated and sustained contraction of the bulk of the bladder smooth musculature. A decrease in outlet resistance occurs with adaptive shaping or funneling of the relaxed bladder outlet. In addition to the inhibition of any continence-promoting reflexes that have occurred during bladder filling, the change in outlet resistance may also involve an active relaxation of the smooth muscle sphincter area through a mechanism mediated by nitric oxide. The adaptive changes that occur in the outlet area are also in part due to the anatomic interrelationships of the smooth muscle of the bladder base and proximal urethra (continuity). Other reflexes elicited by bladder contraction and by the passage of urine through the urethra may reinforce and facilitate complete bladder emptying. Superimposed on these autonomic and somatic reflexes are complex modifying supraspinal inputs from other central neuronal networks. These facilitatory and inhibitory impulses originate from several areas of the nervous system and allow for the full conscious control of micturition in the adult.

Abnormal Function [1–3, 12]

Whatever disagreements exist regarding the details of the anatomy, morphology, physiology, pharmacology, and mechanics involved in both the storage and expulsion of urine by the bladder, agreement is found regarding certain points. First, the micturition cycle involves two relatively discrete processes: bladder filling/storage and bladder emptying/voiding. Second, whatever the details involved, these processes can be summarized succinctly from a conceptual point of view (Tables 2.1 and 2.2).

Any type of voiding dysfunction must result from an abnormality of one or more of the factors previously listed regardless of the exact pathophysiology involved. This division, with its implied subdivision under each category into causes related to the bladder and the outlet, provides a logical rationale for discussion and classification of all types of voiding dysfunction and disorders as related primarily to bladder

Table. 2.1 Bladder filling/storage: the essentials

1. Accommodation of increasing volumes of urine at a low intravesical pressure (normal compliance) with appropriate sensation
2. Bladder outlet closed at rest; remains so during increases in intra-abdominal pressure
3. Absence of involuntary bladder contractions (detrusor overactivity, DO)

Table. 2.2 Bladder emptying/voiding: the essentials

1. Sustained coordinated bladder contraction of adequate magnitude and duration
2. Concomitant adequate lowering of resistance at the level of the smooth and striated sphincter (no functional obstruction)
3. Absence of anatomic outlet obstruction

Table. 2.3 Abnormal lower urinary tract function: simple functional classification

Failure to store

Because of the bladder

Because of the outlet

Failure to empty

Because of the bladder

Because of the outlet

Table. 2.4 Abnormal lower urinary tract function: expanded functional classification of dysfunction

I. Failure to store

A. Because of the bladder

1. Overactivity

- a. Involuntary contractions (detrusor overactivity, DO)
 - Neurologic disease or injury
 - Bladder outlet obstruction (myogenic)
 - Decreased pelvic floor activity
 - Inflammation
 - Idiopathic

b. Decreased compliance

- Neurologic disease or injury
- Fibrosis
- Idiopathic

c. Combination

2. Hypersensitivity

- a. Inflammatory/infectious
- b. Neurologic
- c. Psychologic
- d. Idiopathic

3. Underactivity (with retention and overflow incontinence)

B. Because of the outlet

1. Stress urinary incontinence (SUI)

- a. Lack of suburethral support
- b. Pelvic floor laxity, hypermobility

2. Intrinsic sphincter deficiency (ISD)

- a. Neurologic disease or injury
- b. Fibrosis

3. Combination (SUI and ISD)

C. Combination (bladder and outlet factors)

D. Fistula

II. Failure to empty

A. Because of the bladder (underactivity)

1. Neurogenic
2. Myogenic
3. Psychogenic
4. Idiopathic

B. Because of the outlet

1. Anatomic

- a. Prostatic obstruction
- b. Bladder neck contracture
- c. Urethral stricture, fibrosis
- d. Urethral compression

2. Functional

- a. Smooth sphincter dyssynergia (bladder neck dysfunction)
- b. Striated sphincter dyssynergia
- c. Combination (bladder and outlet factors)

III. Combination

filling/urine storage or to bladder emptying/voiding (Tables 2.3 and 2.4). There are some types of voiding dysfunction that represent combinations of filling and storage and emptying and voiding abnormalities. Within this scheme, however, these become readily understandable, and their detection and treatment can be logically described. For example, the type of abnormal function seen in a patient with suprasacral spinal cord injury after spinal shock has passed represents a combined filling/storage problem (detrusor overactivity) and an emptying one (striated sphincter dyssynergia). Further, using this simple-minded scheme, all aspects of urodynamic, radiologic, and video urodynamic evaluation can be conceptualized as to exactly what they evaluate in terms of either bladder or outlet activity

during filling and storage or emptying and voiding (see Table 2.5). Treatments for voiding dysfunction can be classified as under broad categories according to whether they facilitate filling and storage or emptying and voiding and whether they do so by acting primarily on the bladder or on one or more of the components of the bladder outlet (see Tables 2.6 and 2.7).

Table. 2.5 Using the functional schema to simply categorize urodynamic studies (after Wein [2])

	Bladder	Outlet
Filling/storage	P_{ves}^a P_{det}^b (FCMG ^c)	ALPP ^d
	DLPP ^e	UPP ^f
		FLUORO ^g
Emptying/voiding	P_{ves}^a P_{det}^b (VCMG ^h)	FLUORO ^g
		MUPP ⁱ
		EMG ^j
	Uroflowmetry	
	Residual urine	

In this representation uroflowmetry and residual urine volume integrate the activity of the bladder and outlet during the emptying/voiding phases of micturition

^aTotal intravesical pressure

^bDetrusor pressure

^cFilling cystometrogram

^dAbdominal leak point pressures

^eDetrusor leak point pressure

^fUrethral pressure profile

^gFluoroscopy of outlet

^hVoiding cystometrogram

ⁱMicturitional urethral pressure profile

^jElectromyography of striated sphincter

Table. 2.6 Functional categorization of therapy to facilitate urine storage/bladder filling

I. Bladder
A. Behavioral therapy including any or all of
1. Education
2. Bladder training
3. Timed bladder emptying or prompted voiding
4. Fluid restriction
5. Pelvic floor physiotherapy ± biofeedback
B. Pharmacologic therapy (oral, intravesical, intradetrusor)
1. Antimuscarinic agents
2. Drugs with mixed actions
3. β-Adrenergic agonists

4. Botulinum toxin
5. Calcium antagonists
6. Potassium channel openers
7. Prostaglandin inhibitors
8. α-Adrenergic antagonists
9. Tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors
10. Dimethyl sulfoxide (DMSO)
11. Polysynaptic inhibitors
12. Capsaicin, resiniferatoxin, and like agents
C. Bladder overdistention
D. Electrical stimulation (sacral neuromodulation, posterior tibial and other peripheral nerve stimulation)
E. Acupuncture and electroacupuncture
F. Interruption of innervation
1. Very central (subarachnoid block)
2. Less central (sacral rhizotomy, selective sacral rhizotomy)
3. Peripheral motor or/and sensory
G. Augmentation cystoplasty (auto, bowel, tissue engineering)
II. Outlet related (increasing outlet resistance)
A. Behavioral therapy (see I, A)
B. Electrical stimulation
C. Pharmacologic therapy
1. α-Adrenergic agonists
2. Tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors
3. β-Adrenergic antagonists, agonists
D. Vaginal and perineal occlusive and/or supportive devices, urethral plugs
E. Nonsurgical periurethral bulking
1. Synthetics
2. Tissue engineering
F. Retropubic vesicourethral suspension ± prolapse repair (female)
G. Sling procedures ± prolapse repair (female)
H. Mid-urethral tapes ± prolapse repair (female)
I. Perineal sling procedure (male)
J. Artificial urinary sphincter
K. Myoplasty (muscle transposition)
L. Bladder outlet closure
III. Circumventing the problem
A. Absorbent products
B. External collecting devices
C. Antidiuretic hormone-like agents
D. Short-acting diuretics
E. Intermittent catheterization
F. Continuous catheterization
G. Urinary diversion

Table 2.7 Functional categorization of therapy to facilitate bladder emptying/voiding (after Wein [2])

I. Bladder related (increasing intravesical pressure or facilitating or augmenting bladder contractility)
A. External compression, Valsalva
B. Promotion or initiation of reflex contraction
1. Trigger zones or maneuvers
2. Bladder “training,” tidal drainage
C. Pharmacologic therapy (oral, intravesical)
1. Parasympathomimetic agents
2. Prostaglandins
3. Blockers of inhibition
a. α -Adrenergic antagonists
b. Opioid antagonists
c. Electrical stimulation
1. Directly to the bladder or spinal cord
2. Directly to the nerve roots
3. Intravesical (transurethral)
4. Sacral Neuromodulation
E. Reduction cystoplasty
F. Bladder myoplasty (muscle wrap)
II. Out related (decreasing outlet resistance)
A. At a site of anatomic obstruction
1. Pharmacologic therapy—decrease prostate size or tone
a. α -Adrenergic antagonists
b. 5 α -reductase inhibitors
c. Luteinizing hormone releasing hormone-agonists/antagonists
d. Antiandrogens
2. Prostatectomy, prostatotomy (diathermy, heat, laser), dilation, and fixation
3. Bladder neck incision, resection, dilation, reconstruction
4. Urethral stricture repair, dilation
5. Intraurethral stent
B. At level of smooth sphincter (functional obstruction)
1. Pharmacologic therapy
a. α -Adrenergic antagonists
b. β -Adrenergic agonists
2. Resection, incision, reconstruction
C. At level of striated sphincter (functional obstruction)
1. Behavioral therapy $\pm$ biofeedback
2. Pharmacologic therapy
a. α -Adrenergic antagonists
b. Botulinum toxin (injection)
c. Benzodiazepines
d. Baclofen
e. Dantrolene
3. Urethral overdilation
4. Surgical sphincterotomy

5. Urethral stent
6. Pudendal nerve interruption
III. Circumventing the problem
A. Intermittent catheterization
B. Continuous catheterization
C. Urinary diversion

References

- Wein AJ, Barrett DM. Voiding D+function and dysfunction: a logical and practical approach. Chicago, IL: Year Book Medical; 1988.
- Wein AJ. Pathophysiology and classification of lower urinary tract dysfunction. In: Wein AJ, Kavoussi LR, Novick AC, Parlin AW, Peters CA, editors. Campbell-Walsh urology. Philadelphia, PA: Elsevier/Saunders; 2012. p. 1834–46.
- Wein AJ. Classification of neurogenic voiding dysfunction. J Urol. 1981;125:605–9.
- de Groat WC, Booth AM, Yoshimura N. Neurophysiology of micturition and its modifications in animal modules of human disease. In: Maggi CA, editor. Autonomic nervous system. London: Harwood Academic; 1993. p. 227–90.
- de Groat WC, Downie JW, Levin RM, et al. Basic neurophysiology and neuropharmacology. In: Abrams P, Khoury S, Wein AJ, editors. International consultation on incontinence. Plymouth, UK: Health Publications; 1999. p. 105–54.
- Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. Nat Rev Neurosci. 2008;9:453–66.
- Andersson K-E, Arner A. Urinary bladder contraction and relaxation: physiology and pathophysiology. Physiol Rev. 2004;84:935–88.
- Yoshimura N, Chancellor MB. Physiology and pharmacology of the bladder and urethra. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh urology. Philadelphia, PA: Elsevier/Saunders; 2012. p. 1786–833.
- Zderic SA, Levin RM, Wein AJ. Voiding function: relevant anatomy, physiology, pharmacology and molecular aspects. In: Gillenwater JY, Grayhack JT, Howard SS, Duckett Jr JW, editors. Adult and pediatric urology. Chicago, IL: Chicago Year Book Medical; 2002. p. 1159–219.
- Newman DK, Wein AJ. Managing and treating urinary incontinence. Baltimore and London: Health Professions Press; 2009.
- Zinner NR, Sterling AM, Ritter R. Structure and forces of continence. In: Raz S, editor. Female urology. Philadelphia, PA: WB Saunders; 1983. p. 33–41.
- Wein AJ, Moy ML. Voiding function and dysfunction: urinary incontinence. In: Hanno PM, Malkowicz SB, Wein AJ, editors. Penn clinical manual of urology. Philadelphia, PA: Elsevier/Saunders; 2007. p. 341–478.

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