INTRODUCTION

The urinary tract consists of two mutually dependent components:
• upper tract (kidneys and ureters);
• lower tract (bladder and urethra).

This provides a highly sophisticated system of conduits that converts the continuous involuntary production of urine by the kidneys into the intermittent, consciously controlled voiding of urine (micturition) in appropriate circumstances.

The upper tracts function as a low-pressure distensible conduit with intrinsic peristalsis, which transports urine from the nephrons via the ureters to the bladder. The vesicoureteric mechanism protects the nephrons from damage that might arise from retrograde transmission of back pressure or infection from the bladder.

THE URINARY BLADDER

The bladder has two main functions:
• collection and low-pressure storage of urine;
• expulsion of urine at an appropriate time and in an appropriate place.

Histologically it is made up of three layers:
• an outer adventitial connective tissue layer;
• a middle smooth muscle coat (detrusor muscle), comprising a functional syncytium of interlacing muscle bundles;
• an innermost lining comprised of transitional cell epithelium providing an elastic barrier that is impervious to urine (Figure 2.1).

Innervation
The detrusor muscle is controlled by the autonomic nervous system and is richly innervated by three groups of nerves:
• the principal population is comprised of presumptive cholinergic nerves (identified by their content of the enzyme acetylcholinesterase and demonstrated by the use of electron microscopy to lie in close apposition to muscle cells) — by releasing the neurotransmitter acetylcholine they provide the major motor control of the detrusor muscle;
• the sympathetic innervation comprises a sparse distribution of noradrenergic neurones, which occur in greatest concentration towards
Chapter 2 | Structure and function of the urinary tract

Figure 2.1 Structure of the bladder wall. The bladder wall is comprised of three layers and has a rich innervation of cholinergic, adrenergic, and nonadrenergic noncholinergic sensorimotor nerves. Intramural ganglia allow extensive neural interaction.

the bladder base and are thought to be of principal importance in controlling the vasculature;
- the third population of nonadrenergic noncholinergic (NANC) sensorimotor nerves contains a variety of putative neurotransmitters (principally peptides), which can be identified by immunofluorescent techniques – their precise role in controlling the human bladder is not clear.

The close juxtaposition of these neural populations allows them to interact. To facilitate this there are potential neural links via ganglia at every level from the spinal cord to the target organs (prostate, bladder, sphincters), in particular between the parasympathetic and sympathetic nervous systems.

The spinal segments S2–S4 act via efferent parasympathetic cholinergic neurones to initiate and maintain detrusor contraction. Damage to these spinal segments abolishes the micturition reflex.

After leaving the sacral foramina, the pelvic splanchnic nerves containing the parasympathetic innervation to the bladder pass lateral to the rectum to enter the inferior hypogastric or pelvic plexus. They are joined by the hypogastric nerve containing efferent sympathetic nerve fibres originating from the spinal cord segments T10–L2. When combined they form a plexus at the base of the bladder.

It has been suggested that:
- the pelvic nerves provide the main afferent pathway of the micturition reflex – there is now increasing evidence to suggest that the urothelium and its associated afferent innervation has an important role in the normal control of micturition;
Figure 2.2  **Neural control of the lower urinary tract.** There is extensive interaction within the spinal cord and in paravesical and intramural bladder ganglia (not shown).
sympathetic neuronal pathways in the hypogastric nerves (innervating the trigone) passing to the spinothalamic tracts (bladder and urethral sensation) provide additional afferent information.

The sympathetic nerves provide the main motor control for urethral and prostatic smooth musculature. The somatic pudendal nerve contributes an additional component to the striated sphincter mechanism (Figure 2.2).

**SPHINCTERIC MECHANISMS**

Apart from the obvious anatomical differences (the longer urethra and presence of a prostate gland in men), there are important differences in the histological structure, innervation, and function of the outflow tract between males and females (Figure 2.3).

![Lower urinary tract](image)

**Figure 2.3** Lower urinary tract.

**In males**

In the male there are two important sphincteric mechanisms:
- a proximal 'bladder neck mechanism';
- a urethral mechanism lying at the apex of the prostate (the 'distal sphincter mechanism').

The male bladder neck is a powerful sphincter subserving both the urinary and genital roles, the latter function being of primary importance in preventing retrograde ejaculation.

The distal sphincteric mechanism is also extremely important as evidenced by its ability to maintain continence even when the bladder neck has been rendered totally incompetent by bladder neck incision or prostatectomy. Conversely in patients who have a damaged distal urethral
sphincter (e.g. as in pelvic fracture-associated urethral disruption) continence is maintained by the bladder neck mechanism.

**In females**
The female bladder neck is a far weaker structure than the male bladder neck and can be incompetent, even in nulliparous young women. Urinary continence in women usually relies upon the integrity of the intrinsic urethral sphincteric mechanism. Damage to the innervation of the urethral sphincter (in particular the pudendal nerve) by obstetric trauma predisposes to urinary stress incontinence.

**Ultrastructural findings**
The functional observations for the sphincteric mechanisms are mirrored by the ultrastructural findings.

**Bladder neck**
Ultrastructurally, the bladder neck:
- in males consists of two muscular layers – a powerful inner layer of muscle bundles arranged in a circular orientation containing a rich adrenergic sympathetic nerve supply and an outer layer contiguous with the detrusor muscle and receiving both a cholinergic and adrenergic innervation;
- in females is poorly defined with the muscle fibres having a mainly longitudinal orientation and the predominant innervation being cholinergic.

**Urethral sphincter mechanism**
This is composed of intrinsic urethral smooth muscle and extrinsic striated muscle components and:
- in females it extends throughout the proximal two-thirds of the urethra, being most developed in the middle one-third of the urethra, particularly dorsally;
- in males it is localized to the prostatic apex.

**Extrinsic component of the urethral sphincter**
The efferent innervation of the striated muscle of the extrinsic component of the urethral sphincter arises predominantly from cell bodies lying in a specific area of the sacral anterior horn known as Onuf’s nucleus. Various aspects of the innervation of this sphincter are controversial – not only the neural pathways involved, but also the relative contribution of somatic and autonomic nerves. The limited knowledge available suggests that the pudendal nerve transmits urethral mucosal sensation.

**Prostate gland**
The prostate is made up of smooth muscle and glandular tissue, the proportion of smooth muscle being increased in benign prostatic hyperplasia. This muscle
is controlled by the sympathetic nervous system, which acts by releasing noradrenaline onto $\alpha_{1A}$ adrenoceptors located on prostatic smooth muscle cells.

**MICTURITION REFLEXES**

Before considering the clinical investigation and treatment of disorders of micturition it is first essential to consider the neural mechanisms controlling urinary tract function. Although most contemporary knowledge is based on studies with experimental animals, it is difficult and often misleading to relate the findings from such animal models directly to man. However, data for humans are limited as they can only be obtained from studying clearly defined clinical syndromes and isolated spinal cord lesions.

The pioneering neurophysiologist, Barrington, initially described five reflexes associated with micturition in the cat, to which he added a further two after further study. Two of these reflexes had reflex centres in supraspinal sites (medulla and pons) and caused strong and sustained contractions. He considered that these were essential for normal micturition because bladder contraction and urethral relaxation are not coordinated after experimentally produced high spinal transection. The remaining five reflexes appeared to be confined to the spinal cord. More recently it has been proposed that many interrelated reflexes act upon the sacral micturition centre exerting both excitatory and inhibitory effects.

**URINE STORAGE AND VOIDING**

Urine storage and voiding are two interrelated yet distinct phases of lower urinary tract function.

The bladder and urethra possess intrinsic tone produced by the muscle and connective tissue they contain. At rest, the urethral tone keeps the walls in apposition and aids continence. During filling the walls of the bladder exhibit receptive relaxation (i.e. the vesical lumen expands without resulting in a concomitant rise in intravesical pressure). The extent to which a change in volume ($\delta V$) occurs in relation to a change in intravesical pressure ($\delta P$) is known as the bladder compliance ($\delta V/\delta P$). Factors that contribute to this property are:

- the passive viscoelastic properties of the bladder; and
- the intrinsic ability of smooth muscle to maintain a constant tension over a wide range of stretch.

The other major factor controlling bladder filling is its neural control. During bladder filling afferent activity from stretch receptors increases and passes via the posterior roots of the sacral cord and the lateral spinothalamic tracts to the brain, thereby mediating the desire to void. Activity within the striated component of the urethral sphincter is increased and local spinal reflex activity enhances the activity within striated muscles of the pelvic floor and sphincter to tighten up the bladder outlet mechanisms and so augment continence.
Important local factors facilitating bladder filling include both receptive relaxation and the passive viscoelastic properties of the bladder wall. Conditions that contribute to poor bladder compliance and detrusor instability (see pp. 110–115) include:
- abnormal bladder morphology resulting from collagenous infiltration, hypertrophy, or altered muscle structure (e.g. obstructed bladder); and
- abnormal detrusor smooth muscle behaviour, either primary or secondary to neural dysfunction.

**Initiation and control of voiding**

Once a threshold level of filling has been achieved (which will depend upon circumstances and vary between individuals), increasing afferent activity will start to impinge on consciousness, resulting in awareness that the bladder is filling up. Except during infancy, in health there is complete volitional control over these reflex pathways and voiding will be initiated in appropriate circumstances. Micturition initiated by the cerebral cortex is likely to involve a complex series of bladder–brain stem reflexes.

During voiding:
- urethral relaxation precedes detrusor contraction;
- there is simultaneous relaxation of the pelvic floor muscles; and
- there is accompanying funnelling of the bladder neck.

The mechanism of these changes is not clear. It is likely that:
- increased activity within parasympathetic neurones results in removal of central inhibitory influences acting on the sacral centres; and
- voiding is initiated under the influence of pontine medullary centres.

There is therefore parasympathetically-controlled detrusor contraction associated with a corresponding relaxation of the urethra/prostate/bladder neck complex resulting from reciprocal nerve-mediated inhibition of the sympathetic nerve-mediated outflow.

In addition to these primary actions other important secondary events are:
- contraction of the diaphragm and anterior abdominal wall muscles;
- relaxation of the pelvic floor; and
- specific behavioural changes associated with voiding.

At the end of voiding the proximal urethra is closed in a retrograde fashion, the ‘milkback’ seen at videocystometry. Once these events have been completed, the sacral centres are re-inhibited by the cortex and the next filling cycle starts.

**VESICOURETHRAL FUNCTION**

**Normal function**

Normal function of the human lower urinary tract depends upon integrated coordination of the neural control of the bladder and outflow tract, for which an intact spinal cord is essential.
Chapter 2 | Structure and function of the urinary tract

Under normal circumstances:
• bladder capacity is approximately 500 ml and the bladder empties, leaving no residual urine;
• males void at a pressure of 40–50 cm H₂O and a maximum flow rate of 30–40 ml/s; and
• females void at a pressure of 30–40 cm H₂O and a maximum flow rate of 40–50 ml/s.

The difference between males and females is a consequence of the higher outflow resistance exerted by the male urethra.

Abnormal function
Disordered lower urinary tract function can result from:
• disruption of the normal peripheral or central nervous system (CNS) control mechanisms; and
• disordered bladder muscle function, either primary (of unknown aetiology) or secondary to an identifiable pathology such as prostatic-mediated bladder outflow obstruction.

CLINICAL NOTES

• Patients who have disordered lower urinary tract function in routine clinical practice represent a heterogeneous collection for most of whom there is no identifiable neurological abnormality
• Some of these patients will have a primary neural or muscular disorder (e.g. primary idiopathic detrusor instability) in contrast to postobstructive secondary detrusor instability where the major aetiological factor is likely to be peripheral disruption of local neuromuscular function.

Disruption of normal peripheral or central nervous system control mechanisms
A neurological classification is invaluable for counselling and can be of useful prognostic significance. Certain characteristic patterns – peripheral denervation, suprasacral spinal cord lesions, and cerebral (suprapontine) lesions – can be identified (see below).

Peripheral denervation
The clinical picture of peripheral denervation depends upon the extent of denervation. Complete lesions decentralize the lower urinary tract and although ganglionic activity may persist, an acontractile bladder will result with an inactive urethra. Subsequent continence is governed by the functional competence of the bladder neck mechanism. The urethra has a fixed resistance and bladder
emptying depends upon abdominal straining or manual compression. Partial lesions often result in detrusor hyperreflexia.

**Suprasacral spinal cord lesions**
If the spinal cord is transected above the fifth lumbar segment, a ‘cord bladder’ develops. A principal feature of this lesion is loss of coordinated detrusor–sphincter behaviour, which results in simultaneous contraction of the detrusor and urethral sphincter (detrusor–sphincter dyssynergia). Sphincter contractions are not usually prolonged throughout the period of detrusor action, so there is intermittent voiding, but also urine retention. Voiding function can be particularly ineffective in people who have lesions of the thoracolumbar cord, and in these people low compliance is an important feature.

**Cerebral (suprapontine) lesions**
Lesions of the midbrain rarely result in disturbances of continence and micturition. It is likely that this is due to:
- the bilateral representation of nuclei at this level; and
- the poor prognosis of patients who have extensive lesions.

Damage to the basal ganglia results in a reduced threshold for the transmission of impulses through the reticulospinal tracts controlling micturition. The typical picture is therefore of involuntary bladder contractions, which occur in people who have Parkinson’s disease and following cerebrovascular thrombosis or haemorrhage.

Lesions of the cerebral cortex, in particular involving the inner surface of the cerebral hemispheres or the frontal cortex, can result in incontinence. It is felt that these patients lose the centrally mediated inhibition of the pontine voiding reflex resulting in involuntary bladder contractions and urge incontinence.

**CLINICAL NOTES**

Many urinary disorders seen in clinical practice may have a neurological cause, but a classification based on specific abnormalities and in particular the site of a neurological lesion is not practical because:
- the aetiology and pathogenesis of many disorders is at present unclear;
- lesions are often difficult to locate and once located can be difficult to relate to the neurological signs (e.g. multiple sclerosis); and
- different lesions can produce identical functional changes in the lower urinary tract.

**DISORDERS OF THE LOWER URINARY TRACT**

Disorders of the lower urinary tract can best be subdivided into:
disorders of sensation; and
- disorders of motor function.

Each of these may affect:
- the detrusor muscle; or
- the sphincter-active bladder outflow tract (bladder neck mechanism, distal urethral sphincter mechanism, prostate).

The detrusor muscle and the sphincter-active bladder outflow tract may be normal, overactive or underactive.

**Disorders of sensation**
These disorders represent an important poorly understood group of conditions where investigation is limited by:
- limited knowledge about the structural and physiological basis for the perception of sensation in the lower urinary tract; and
- the subjective nature of sensation.

Attempts to quantify sensation have included the use of objective or semi-objective tests for sensory function such as evoked potentials and electrical threshold studies.

At present disorders of sensation are usually assessed by asking the patient about voiding pattern and any discomfort felt, based on clinical questioning or cystometry.

Because most sensory disorders are idiopathic, diagnosis of such a disorder can only be considered after other vesical or urethral pathologies (tumour, stone, infection, abnormal detrusor function) have been excluded.

In general terms, sensation can be subdivided as normal, hypersensitive, hyposensitive, and absent.

**TERMINOLOGY: DISORDERS OF SENSATION**

- **First sensation of filling:** very subjective; a variable and unreliable symptom
- **First desire to void:** can be difficult to interpret; very subjective
- **Strong desire to void:** indicates maximum bladder capacity and signals the end of bladder filling during cystometry
- **Pain:** pain during bladder filling or micturition is abnormal; its site and character should be noted, as well as the volume at which it occurred.

**Disorders of detrusor motor function**
Cystometry is needed to assess detrusor function and not only may detrusor function differ during filling and voiding, but the classification may change between these two phases.
Detrusor function should be considered in the context of coexisting urethral function, but is often the primary cause of marked functional disruption.

Detrusor function may be:
- normal (stable);
- overactive;
- underactive (hypocontractile); or
- acontractile.

**TERMINOLOGY: DISORDERS OF DETRUSOR MOTOR FUNCTION**

- **Stable detrusor function**: during filling bladder capacity increases in volume without a marked corresponding rise in pressure
- **Normal detrusor contractility**: normal voiding occurs as a result of a sustained detrusor contraction, which can be initiated and suppressed voluntarily and results in complete bladder emptying over a normal timespan; the magnitude of the recorded detrusor pressure rise depends upon outlet resistance
- **Overactive bladder**: a descriptive term that is applied to the combination in part or together of the lower urinary tract symptoms of urgency plus frequency, nocturia or urge incontinence
- **Overactive detrusor function**: involuntary detrusor contractions during bladder filling, either spontaneous or provoked by rapid filling (provocation cystometry), provocative tests (hand washing, heel bouncing, alteration in posture, exercise, or coughing)
- **Unstable detrusor**: detrusor that is objectively shown to contract either spontaneously or on provocation during the filling phase during an attempt to inhibit micturition; it may be asymptomatic and it occurs in the absence of a documented neurological disorder
- **Detrusor hyperreflexia**: detrusor hyperactivity in the presence of a documented neurological disorder
- **Detrusor instability**: detrusor hyperactivity in the absence of a documented neurological disorder
- **Normal compliance**: little or no rise in detrusor pressure during normal bladder filling; at present there are insufficient data to adequately define normal, high, and low compliance
- **Low compliance**: gradual rise in detrusor pressure during bladder filling; usually describes a poorly distensible bladder (e.g. a shrunken fibrotic bladder complicating interstitial cystitis or after radiotherapy); detrusor instability and hyperreflexia also may be associated with low compliance
- **Underactive (hypocontractile) detrusor function**: detrusor contraction during micturition is inadequate to empty the bladder
• **Acontractile detrusor:** no contractile activity on urodynamic investigation
• **Areflexic detrusor:** acontractility resulting from a neurological abnormality
• **Decentralized detrusor:** a specific type of areflexic detrusor that occurs with lesions of the conus medullaris or sacral nerve outflow, where the peripheral ganglia in the wall of the bladder are preserved and the peripheral nerves are therefore intact but ‘decentralized’; characterized by involuntary intravesical pressure fluctuations of low amplitude, sometimes called ‘autonomous waves’
• **Genuine stress incontinence:** is said to occur when there is demonstrable incontinence associated with a rise in intra-abdominal pressure in the absence of detrusor overactivity. It is due to intrinsic urethral sphincteric weakness.
• **Mixed incontinence:** is a situation where there is a combination of detrusor overactivity and urethral sphincteric weakness

**Bladder outflow tract dysfunction**
The urethral closure mechanisms, including intrinsic urethral muscle and the sphincteric mechanisms (bladder neck and distal urethral) are best considered separately according to the phase of bladder function (either storage or voiding).

Urethral function during storage may be:
• normal – there is a positive urethral closure pressure that is sufficient to maintain continence in the presence of increased intra-abdominal pressure;
• incompetent – there is leakage, even in the absence of detrusor contraction; it may result from damage to the urethra or the associated sphincteric mechanisms;
• underactive; or
• absent.

Urethral function during micturition may be:
• normal – the urethra opens to allow the bladder to be emptied;
• obstructive due to overactivity – the urethral closure mechanisms contract against a detrusor contraction or fail to open on attempted micturition – when this occurs in the absence of documented neurological disease it is known as ‘dysfunctional voiding’;
• obstructive due to a mechanical problem – this is uncommon in women, but is the most common cause of bladder outflow tract dysfunction in the male population, usually due to urethral stricture or prostatic enlargement; mechanical obstruction can arise as a consequence of anatomical factors (e.g. prostatic enlargement due to adenomatous hyperplasia) or neural control mechanisms (e.g. providing a functional
basis for the relief of obstruction by \( \alpha \)-adrenoceptor blockade of the prostate). In this context it is notable that in recent years it has been increasingly recognised that an important component of prostatic obstruction results from smooth muscle contraction within the pathologically enlarged prostate.

**Detrusor–urethral dyssynergia**
In detrusor–urethral dyssynergia there is synchronous contraction of the detrusor and urethra. It can be subdivided depending upon the structures involved into detrusor–bladder neck dyssynergia and detrusor–sphincter dyssynergia.

**Detrusor–bladder neck dyssynergia**
This refers to a detrusor contraction in the presence of incomplete bladder neck opening on micturition. It is not uncommon in the general population, and is a common cause of voiding dysfunction in younger males. It is thought to be a congenital abnormality, and commonly presents in the third and fourth decades of life.

**Detrusor–sphincter dyssynergia**
Detrusor–sphincter dyssynergia (DSD) describes a detrusor contraction occurring at the same time as an involuntary contraction of the urethral or periurethral striated smooth muscle.

Obstructive overactivity of the striated urethral sphincter muscle may occur in the absence of detrusor contraction, but is not DSD. This condition is uncommon in the general population, it affects women in particular and is most commonly seen in association with polycystic ovary disease.

Detrusor–sphincter dyssynergia is usually associated with neurological disorders and the diagnosis needs to be treated with caution in the absence of a documented neurological deficit.