NEUROPHYSIOLOGY OF THE BLADDER¹

By W. KEITH YEATES, M.D., M.S., F.R.C.S.

Department of Urology, Newcastle General Hospital

So little is understood about the function of smooth muscle and of the central nervous system that a presentation on bladder physiology can be little more than a series of working hypotheses linking known facts, and inevitably has a large content of personal concepts.

TELEOLOGICAL ASPECTS OF BLADDER FUNCTION

1. Frequency. Micturition should not interfere with sleep during the night, nor unduly with ordinary activities during the day. Basically the number of acts of micturition during a given time depends on the urinary output during that time divided by the functional capacity of the bladder. On a fluid intake dictated by thirst—as opposed to pleasure or habit—the functional capacity must accommodate a night's output of urine; which in turn means that the capacity is large enough for the necessary acts during the day to correspond approximately to rest periods imposed by hunger, *i.e.* to meal times.

2. Avoidance of Urinary Contamination of the Skin. The detailed requirements for this very obvious—and hence rarely stated—requirement include:

- (i) the adoption of a micturition posture, which in the human requires quite intricate limb movements;
- (ii) a bladder contraction, a urethral calibre, and a meatal configuration to cast and direct the urine away from the skin.

3. Micturition in a Sociably Acceptable Site. This requirement necessitates:

- (i) the patient must understand what is a sociably acceptable site; and
- (ii) must be mobile enough to get there.

Postponement of micturition until the preliminary requirements of site selection, mobility and posturing have been achieved is an essential feature in the maintenance of continence.

These features can be summarised in the form of a diagrammatic filling-and-emptying cystometrogram—the 'micturition cycle' (fig. 1).

Nearly all these mechanisms are dependent on connections with and the activity of the central nervous system. The one exception is the basic bladder tone which is represented as a low (about 1/50) pressure gradient on filling; but even the tone can be secondarily affected by neurogenic disorders, *e.g.* overdistension for any reason decreases, and hypertrophy secondary to outlet obstruction increases, the pressure gradient.

¹ Symposium on Special Aspects of Urology, University of Liverpool, September 1973.

FIG. 1
The micturition cycle.

FIG. 2
Diagram showing increases in intra-abdominal pressure are applied to both the bladder and the intra-abdominal part of the urethra.

Continence during the Filling Phase. As the bladder fills, continence is at first maintained independently of the nervous system owing to the combination of the low pressure gradient, and the architecture of the bladder neck which is designed so that the outlet is closed at rest.

The total intravesical pressure at any time depends on the sum of the extravescical (extrinsic) pressure and the intrinsic pressure produced by the bladder tone or bladder contraction. Besides the rises in intra-abdominal pressure produced by straining, coughing, sneezing, etc., the extrinsic pressure on the bladder is also increased in the vertical posture by the weight of the abdominal contents.

To prevent leakage during the filling phase when the intravesical pressure is increased, the resistance of the bladder outlet must also be increased. This is effected by:

- (i) reflex contraction of the pelvic floor muscles, particularly the levatores ani;
- (ii) the rise in intra-abdominal pressure itself, which not only compresses the bladder but is also applied to the intra-abdominal part of the urethra, *i.e.* to the whole of the prostatic and the upper part of the membranous urethra in the male, and the upper two-thirds of the urethra in the female, so maintaining the apposition of its walls (fig. 2).

Straining is therefore not the mechanism designed to empty the bladder—in fact quite the reverse. Urine flow cannot be initiated by straining unless the bladder neck is open beforehand—either congenitally or as the result of bladder neck resection, or from its being held open by a maintained bladder contraction against resistance at the level of the pelvic floor. In some cases, however, straining actually increases the urethral resistance by setting off reflex contractions of the pelvic floor muscles.

The Postponement Phase. This begins with the desire to micturate and ends with the appearance of urine at the external meatus.

The existence of the postponement phase therefore depends initially on the reception of the desire to micturate; and the value of the phase is dependent on the suppression of bladder activity until the preparations for micturition previously mentioned have been achieved.

The Desire to Micturate (fig. 3). The most important impulses concerned with reflex micturition obviously must arise in association with bladder distension. These impulses have been shown (Iggo, 1955) to be associated with tension in the bladder wall, and consideration of clinical states suggests that the intensity of stimulation is related to the rate of rise of this tension rather than to the degree of the tension itself.

Although reflex arcs which can produce bladder contractions are—at least potentially—present in the sacral segments of the spinal cord, activity through this level does not result in a coordinated act of micturition. Both experimental (Tang, 1955) and clinical evidence strongly suggest that the most important level of reflex bladder activity is about the level of the hypothalamus which can be thought of as the functional centre of micturition.

The impulses from the bladder pass through the 2nd, 3rd and 4th sacral

nerves up the spinal cord in about the equatorial plane to the region of the hypothalamus where they set up a central excitatory state (C.E.S.).

Other impulses concerned with the charging of this C.E.S. arise from the same (S_{2,3,4}) segments—from the mucosa of the bladder, or the urethra, or from the perineal skin. Confirmation of the reality of these impulses is illustrated by the facts that anaesthetising the perineal skin or urethra or bladder mucosa increases—and stimulation of these sites decreases—the functional capacity of the bladder.

Cold, and the sound of running water, are particularly effective stimuli.

The tension of the C.E.S. can be thought of as being suppressed involuntarily about the level of the basal ganglia—'unconscious inhibition' (fig. 4).

FIG. 3

Fig. 3.—Components in the desire to micturate ('D.V.').

FIG. 4

Fig. 4.—Central control of micturition. C.E.S.—central excitatory state.

When the accumulated tension in the C.E.S. has risen to a certain degree, radiation to the cerebral cortex occurs, producing the desire to micturate.

The response to this initial awareness of bladder distension has almost invariably to be re-inforcement of the unconscious inhibition from the basal ganglia by conscious inhibition from the cerebral cortex until preparations for micturition—site selection, walking to this site, and adopting a micturition posture—have been completed. In Man all these latter activities are cortical in origin; in addition, the mechanical ability to carry out limb movements is also required.

Urgency of micturition (sometimes ending in precipitancy) may therefore result from either shortening of the postponement phase by excessive stimulation or defective inhibition on the one hand, or by excessive lengthening of the time required for the preparations on the other.

Another way (*vide* sensory disorders, fig. 6) in which the postponement phase may be shortened is by delay in reception of the desire to void until nearer—or after—the onset of the bladder contraction.

Initiation of Micturition (fig. 5). When there is adequate tension in the C.E.S. all that is required to initiate micturition is the removal of inhibition, and this is the mechanism usually postulated. However, micturition can be initiated voluntarily before there is much bladder distension, *i.e.* before the development of the desire to void. The simplest concept of this mechanism is that the cerebral

FIG. 5

Fig. 5.—Coordinated micturition.

FIG. 6

Fig. 6.—Hypaesthesia. Sites of dysfunction shown in dotted oval (deficiencies of sensation and inhibition) and circle (deficiency only in sensation) with diagrammatic cystometrograms alongside.

cortex can itself directly charge the 'centre' (fig. 4), which it then releases to produce micturition.

Co-ordinated Micturition (fig. 5). The mechanism of normal micturition is the production of a sustained powerful bladder contraction coordinated with relaxation of the pelvic floor muscles. This coordination appears to require the presence of the hypothalamus.

The maintenance of the bladder contraction around an ever-decreasing volume of contents requires a continuing discharge of impulses from the central nervous system. Adequate accumulation of impulses in the 'centre' initially, and production of afferent stimuli from the contracting bladder itself, and efficient conduction in the tracts in the central nervous system are all of manifest importance.

The opening of the bladder neck is obviously closely associated with the contraction of the bladder. Although the details of the mechanism are not entirely agreed, the order of the activity is: relaxation of the pelvic floor so that the bladder neck descends, followed by contraction of the bladder with progressive opening of its outlet. These movements are intimately correlated with further relaxation of the pelvic floor muscles.

At the end of micturition the mechanisms are reversed and the bladder neck rises and closes. The urethra is emptied by ejaculatory contractions of the external sphincter acting synergically with the bulbospongiosis.

The pelvic floor muscles normally act partly independently so that the activity found on monitoring of the external anal sphincter may not be truly representative of the activity of the external urethral sphincter or levator ani. However, in extensive spinal cord lesions these muscles tend to act *en masse*.

DISORDERS OF BLADDER FUNCTION

Nearly all bladder dysfunctions are the result of either local abnormality, neurological disorders, or the effect of drugs. It should be noted that the presence of more than one cause of bladder dysfunction is a common occurrence. For example, neurological disorders are commonly associated with prostatic enlargement, and sometimes (e.g. Parkinson's disease) there is a combination of a neurological disorder, the administration of anticholinergic drugs and prostatic obstruction.

Classification of Neurogenic Disorders of the Bladder. No classification is of course entirely satisfactory, but the following scheme provides a basis for considering the various lesions, and can be applied in the understanding and management of most clinical states.

<i>Single lesions</i>	<i>Combined (sensory, inhibition, motor) lesions</i>
1. Sensory	1. Peripheral N.S.
(a) deficiency	(a) pelvic nerves
(b) excess	(b) cauda equina
2. Inhibition	2. C.N.S.
(a) unconscious	(a) below hypothalamus: conus, cord
(b) conscious	(b) above hypothalamus
3. Motor	
(a) deficiency	
(b) excess	

Sensory Lesions. (a) *Deficiency.* Deficiency in receiving the desire to micturate may be the result of deficiencies in the production, the conduction, or the final reception of the stimuli.

The commonest cause of *failure of production* of appropriate stimuli is the inability of the bladder to distend due to outlet weakness, or due to the presence of a fistula. At the other extreme, chronic overdistension of the bladder results in relatively little change in the rate of increase in tension for a given amount of input of urine; this results in a vicious circle of further overdistension and further decrease in the production of stimuli.

Deficiencies of conduction are most commonly seen in lesions of the posterior nerve roots; in the past the commonest cause of this was tabes dorsalis, but now possibly the most commonly seen cause is the result of diabetic neuropathy, though the exact correlation has not been proved.

Lesions of the sensory tracts in the spinal cord or brain, or failure of the reception in the cerebral cortex, automatically result in excessive postponement of micturition and the institution of the vicious circle previously noted with the final result of chronic retention. Chronic retention which is the result of posterior nerve root lesions is usually at low tension, as demonstrated by the pyelograms usually showing no dilatation of the upper urinary tract; presumably this is due to an associated atonia of the muscles of the pelvic floor.

Partial lesions or functional disorders of the afferent fibres above the hypothalamus (fig. 6) prevent the transmission of stimuli from the C.E.S. to the cortex until a higher tension than usual has been built up, *i.e.* until later in bladder filling—often it seems until the actual onset of the evacuating bladder contraction, which provides maximum stimulation. The postponement phase is therefore shortened. This dysfunction ('hypoesthetic urgency') could explain the syndrome or urgency during the day combined with incontinence during sleep. It is probably the most important factor in the enuretic syndrome of childhood.

(b) *Excess.* As previously noted, the stimuli concerned with building up the C.E.S. may arise from the bladder muscle or from the mucosa or skin supplied by the 2nd, 3rd and 4th sacral nerves. Excessive stimulation may therefore arise as the result of bladder hypertrophy, cystitis, urethritis, vulvitis and perineal irritation, *e.g.* from threadworms etc.

The effect of deficient or excessive stimulation must be considered in relation to the activity of the inhibitory mechanisms. If these are normal, the usual result is increased reflex activity producing frequency by decreasing the functional bladder capacity. Depending on the intensity of the stimulation there is a degree of urgency, but in the presence of a normal inhibitory mechanism, actual precipitancy occurs only from very intense stimulation.

Deficiency of Inhibition. (a) *Unconscious.* Some patients with Parkinson's disease or other lesions of the basal ganglia have frequency, urgency and sometimes precipitancy which seems obviously due to a deficiency of inhibition. Murnaghan (1961) reported the effects of stereotactic surgery in cases of Parkinson's disease.

The frequency and part of the urgency element commonly present in children with enuresis seem to be attributable to delay in the development of unconscious inhibition. In some individuals the incontinence during sleep (attributed above to deficiency in conduction of sensation from the hypothalamus to the cortex) disappears, leaving the patient with diurnal frequency and urgency as the residual disability, and occasionally when there has been no history of nocturnal incontinence there is persistent life-long frequency and urgency. These symptoms appear to be attributable to congenital deficiency of unconscious inhibition.

(b) *Conscious.* Patients with lesions of the frontal lobe (most commonly seen in senile degenerations but also in some cases following head injury or in the presence of a cerebral tumour) receive the desire to micturate but are unable to prevent the onset of micturition. As in the disorders of the basal ganglia the bladder-emptying mechanism is quite normal as the coordinating mechanisms from the hypothalamus are intact. In cases of deficient inhibition without sensory

disorders the individual is wakened by the desire to void which distinguishes this type of urgency from the urgency due to hypaesthesia.

Motor Disorders. (a) *Deficiency.* Pure motor disorders are very rarely seen except in cortical dysfunction. Inability to initiate micturition when the bladder is not distended is most commonly seen in normal individuals in the 'command' performance before taking the post-evacuation film in an intravenous pyelogram series. Difficulty in initiating micturition even when there is adequate bladder filling, is seen in the functional disorder of nervous hesitancy. Difficulty in initiating micturition is very common in multiple sclerosis; there is a number of possible mechanisms for neurogenic hesitancy in this condition, but some would seem to be of cortical origin.

(b) *Excess.* Excessive stimulation of the micturition mechanisms is seen in giggling incontinence and in epilepsy. These disorders can also be thought of as being due to the removal of inhibition, but the incontinence is so accurately related to emotion or to the fit that the incontinence certainly occurs on some occasions when the bladder is not distended, so that active stimulation of micturition would seem to be the mechanism.

Combined Lesions (sensory, inhibition, motor). 1. **Peripheral Nervous System.** (a) *Pelvic Nerves.* Lesions of the pelvic nerves (affecting both the sensory and motor fibres) sometimes occur during excision of the rectum or radical hysterectomy.

(b) *Cauda Equina* (fig. 7). The vast majority of these lesions result from spinal injury. They usually appear to be mixed motor and sensory lesions, but it should be noted that the cauda equina is made up of long nerve roots so that the sensory and motor fibres are in fact separated above the intervertebral foramina.

The basic features of both these groups are insensitivity of the bladder and the absence of reflex activity. The bladder neck therefore remains closed. Transurethral resection of the bladder neck in these cases makes abdominal wall straining effective by converting the intra-abdominal part of the urethra into an extension of the bladder cavity.

2. **C.N.S. Below the Hypothalamus.** *Conus.* Lesions of the conus are most commonly due to trauma but a plaque in the conus in multiple sclerosis often occurs.

The effects are very similar to those of the cauda equina lesion. A frequent complicating factor in the management of the patient with multiple sclerosis is poor abdominal straining power.

Cord: Sudden lesions of the spinal cord above the conus result at first in spinal shock with the absence of bladder contraction reflexes. The pelvic floor reflexes recover almost immediately (Gibbon, 1966), but in the majority of individuals reflex bladder activity through the conus develops only after a few weeks or months. There are, however, some individuals in whom the conus appears to remain inactive. This can in some cases be attributed to an ischaemic degeneration of the cord below the level of the lesion, but in others this explanation is not valid, and it is tempting to regard the bladder contraction reflexes through the conus as only vestigial in Man—some individuals being incapable of redeveloping bladder reflexes through this level.

The mechanical problem of the absence of both bladder contraction and abdominal-wall straining power is very similar to that in the conus lesions in multiple sclerosis mentioned above.

As previously noted, bladder contraction reflexes below the hypothalamus are not coordinated with reciprocal relaxation of the pelvic floor muscles which therefore act as a functional obstruction (fig. 8). As a result there is bladder hypertrophy

Fig. 7.—Diagram of effects of complete cauda equina lesion. Arrows from rectangles represent straining by diaphragm and abdominal wall.

Fig. 8.—Diagram showing the effects of complete lesion of spinal cord.

and frequently incomplete bladder emptying, the residual urine being at high tension.

Patients with multiple sclerosis may have retention of urine due to a variable proportion of interference with the tracts and 'centres' concerned with bladder reflexes and spasm of the pelvic floor. The greater the element of outlet obstruction the greater is the chance of the disordered mechanism being palliated by procedures to weaken the bladder outlet, *e.g.* external sphincterotomy.

Above the Hypothalamus. Bladder sensations, inhibition, and the initiation of micturition may all be affected in variable degrees by dysfunctions or lesions above the hypothalamus. For example, in the enuretic syndrome dysfunction there

are deficiencies of both sensation and inhibition. Head injuries, vascular accidents, tumours and multiple sclerosis may all produce mixed disorders of bladder function in various combinations and of variable severity.

The emptying mechanism, being coordinated at hypothalamic level, is usually intact.

Somatic Aspects of Neurogenic Bladder Dysfunction. Evacuation of the bladder is not the only aspect of neurogenic disorders of micturition.

Many of these disorders are complicated by associated disabilities of mobility and posturing, which may determine the urological management.

Cortical lesions may remove the ability to appreciate what is a socially acceptable site for micturition and result in disorders of behaviour. Finally, both the diagnosis and the management of cases of neurogenic dysfunction of the bladder may be complicated by associated deficiencies of hearing or speech which prevent adequate communication between the patient and the medical or nursing staff.

SUMMARY

Normal bladder function requires not only coordination of bladder contraction with relaxation of the pelvic floor, but also the somatic activities of mobility and posturing.

Continence depends on the ability to postpone micturition until these requirements have been achieved.

The mechanisms concerned in the phases of bladder function and in bladder dysfunctions are presented as working hypotheses.

Acknowledgement is made to the Annals of the Royal College of Surgeons of England for the use of Figs. 1, 2, 3, 5, 7 and 8.

ZUSAMMENFASSUNG

Normale Blasenfunktion bedarf nicht nur der Koordination der Blasenkontraktion und Relaxation des Beckenbodens sondern hängt auch von somatischer Aktivität und Körperlage ab.

Kontinenz hängt ab von der Fähigkeit, Miktions zu verzögern bis diese Forderungen erfüllt sind.

Die Mechanismen betreffend der Phasen der Blasenfunktion und Blasendysfunktion werden als Arbeitshypothese beschrieben.

RÉSUMÉ

Une fonction vésicale normale requiert non seulement la coordination de la contraction de la vessie avec une relaxation du plancher pelvien, mais aussi des activités somatiques de mobilité et de posture. La continence dépend de la possibilité de retarder la miction jusqu'à ce que ces conditions aient été obtenues. Les mécanismes concernés dans les phases de la fonction vésicale et dans les dysfonctions vésicales sont présentées comme hypothèses de travail.

REFERENCES

- GIBBON, N. O. K. (1966). Management of the bladder in acute and chronic disorders of the nervous system. *Acta Neur. scandi.* Suppl. 20, 42, 135.
 IGGO, A. (1955). Tension receptors in the stomach and the urinary bladder. *J. Physiol.* 128, 593.
 MURNAGHAN, M. F. (1961). Neurogenic disorders of the bladder in Parkinsonism. *Brit. J. Urol.* 4, 403.
 TANG, P. C. (1965). Levels of brain stem and diencephalon controlling micturition reflex. *J. Neurophysiol.* 18, 583.