Pathophysiology of urinary incontinence

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Abstract

Urinary incontinence is a condition with multi-factorial aetiology and a complex pathophysiological basis. However, the underlying principles are relatively simple. In this article we consider these pathophysiological elements in separate sections to emphasise how they interact to effect a change in lower urinary tract pressures during different phases of the micturition cycle.

The interstitial cells have a key sensory role in the bladder, with much research currently taking place to investigate their exact function. Neural pathways, by comparison, are relatively well established and interactions between the pontine micturition centre (PMC) in the brain stem and the sacral micturition centre (SMC) in the sacral spinal cord, with voluntary control from higher centres, provide neurological control of the lower urinary tract. Depending on the level of a neurological deficit or injury, certain recognizable patterns of bladder dysfunction can be identified.

Mechanical factors — the pelvic floor, striated sphincter muscles and smooth muscles of the bladder and urethra — also play a major role in maintaining normal continence.

Dysfunction of any of these elements can cause, to varying degrees, a loss of urethral pressure, a rise in bladder pressure, or both. This imbalance results in incontinence. An understanding of this principle, and the pathophysiological mechanisms behind it, will help guide investigation and treatment choices to best manage patients with this unfortunate condition.

Keywords Bladder; lower urinary tract; neuro-urology; pathophysiology; pelvic floor; pressure; urinary incontinence

Introduction

Urinary Incontinence (UI) is defined by the International Continence Society as the complaint of any involuntary leakage of urine.[1] There are a number of factors that may influence the reported prevalence of UI, including sampling frame, response rates, threshold definitions, types of UI and survey methods. But broadly speaking the prevalence of UI in the general population appears to be in the range of 30—60% in middle-aged and older women, with the condition being twice as prevalent in women as in men.[2]

The cause of UI can be multi-factorial, and understanding the pathophysiological mechanisms requires an understanding of the relevant anatomy, physiology, neural control and biochemistry of the lower urinary tract. In this article we will explore the pathophysiological mechanisms underlying urinary incontinence but also revisit the relevant normal anatomy and physiology, as pertains to continence, before describing the abnormal.

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Bladder wall physiology and neuromuscular control

The bladder wall and interstitial cells

The main purpose of the urinary bladder is to receive urine from the kidneys and act as a compliant pouch to store that urine, until such time as it is socially appropriate and convenient to void. Structurally it is made up of interwoven fibres of detrusor muscle that make up the body of the bladder, and specialized smooth muscle fibres within the detrusor that arise from a distinct embryological source. The muscle layers are lined internally by an inner urothelium that acts as a protective layer. The bladder urothelium is distensible along with the bladder muscle and forms an effective blood—bladder barrier to prevent uraemia.[3] Deep to the urothelium are found the interstitial cells, which have recently been proposed to be the cells responsible for 'pacemaking' activity in the bladder.[4,5] Two types of interstitial cells have been identified — the sub-urothelial interstitial cells (or myofibroblasts) and the intra-detrusor interstitial cells. These cells differ in molecular constitution and neurotransmitter content, but M2 and M3 muscarinic receptor activity of sub-urothelial interstitial cells have been found to correlate with urgency scores in humans,[6] and their position makes them ideally situated to modify feedback mechanisms of ATP and acetyl choline (ACh) between the urothelium and nerve endings.[7] The intra-detrusor interstitial cells can be spontaneously active, so possibly have the pacemaker role, and they also demonstrate cGMP activity.

Neurophysiology

The bladder and urethra are influenced by all three neural systems — sympathetic, parasympathetic and somatic (Figure 1). They innervate the bladder through the pelvic plexus, formed by contributions of the hypogastric (sympathetic) (T10-L2) and pelvic (parasympathetic) (S2—S4) nerves as well as somatic nerves. Sympathetic nerves release noradrenaline and innervate the external urethral (rhabdo) sphincter, the excitatory α-adrenergic response resulting in an increase in muscular tone and thereby outlet resistance. Being a striated muscle this external sphincter is under a degree of voluntary control. There is also evidence of a sympathetic reflex whereby bladder stretch results in stimulation of β-adrenergic receptors in the detrusor that enhance bladder relaxation and inhibit parasympathetic activity.

The parasympathetic nerves innervate the detrusor and via ACh release stimulate detrusor contraction. Autonomic nerves are both under higher control, mainly from the excitatory pontine micturition centre (PMC), located in the brain stem, which causes detrusor contraction by parasympathetic excitation and simultaneous external sphincter relaxation through sympathetic inhibition. The PMC is normally under inhibitory influence from the frontal lobes and cingulate gyrus via the peri-aqueductal grey (PAG), and these centres are responsible for determining the 'socially acceptable and convenient' aspect of normal initiation of voiding.

The main control centres of bladder function are the pontine micturition centre (PMC) mentioned above, and the sacral

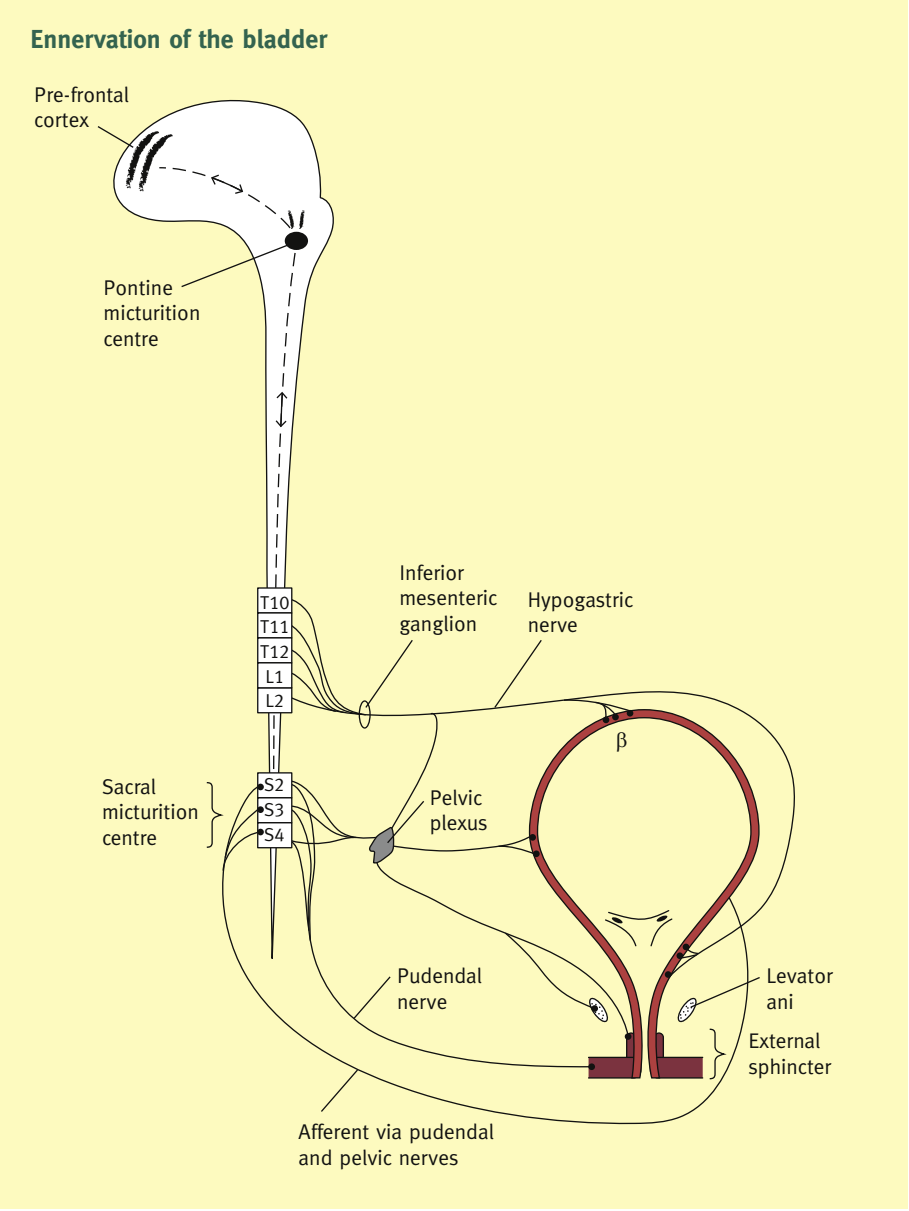

Figure 1

micturition centre (SMC). The SMC is located at S2–S4 spinal levels and communicates with the PMC via spinothalamic tracts. It also has afferent inputs via the pelvic nerves as well as motor output via parasympathetic nerves. The clinical effects of neurological lesions affecting bladder function can largely be determined by assessing whether the main lesion affects the pathway above the PMC, between PMC and SMC, or involves the SMC and lower pathways.

The normal filling and voiding cycle

The bladder performs a number of physiological functions, but basically it serves to store a convenient amount of urine without significant rise in pressure until such time as it is socially acceptable to void, and without itself being damaged by the toxic substances present in the urine it holds. To be able to do this it has some inherent properties and features.

- Compliance – the net-like arrangement of detrusor fibres and the poor electrical coupling between the muscle cells results in the visco-elasticity of the bladder and absence of tetanic contractions that are seen in other smooth muscles of the gastrointestinal tract and uterus.[8]
- Protective urothelium – which forms the effective blood–bladder barrier alluded to earlier, and protects the inner layers of the bladder wall from the toxic effects of prolonged contact with urine.
- Co-ordinated neuronal control – resulting in synchronous activation of smooth muscles and relaxation of striated muscles causing detrusor contraction, bladder neck opening and funnelling, and sphincter relaxation to effect voiding. Neural switches are reset at the end of the void to revert to baseline striated muscle tone (contracted sphincter) and relaxed smooth muscle (bladder neck and wall).