Pathophysiology of urinary incontinence

Michel Wyndaele

Hashim Hashim

Abstract

Urinary incontinence, or the complaint of involuntary loss of urine, is a debilitating condition of the lower urinary tract with a potentially significant impact on a patient's physical and mental wellbeing and on their functioning and place in society. Due to the high prevalence of this disorder, the economic burden on healthcare systems worldwide is enormous. Urinary incontinence has a high prevalence in women, but men can be affected as well after a radical prostatectomy or when suffering from chronic urinary retention. Stress, urgency and mixed urinary incontinence are the most common types of urinary incontinence, but other types exist as well. The pathophysiological mechanisms behind these different types of urinary incontinence have been studied extensively. New insights allow for the development of improved diagnostic and therapeutic strategies and ultimately in the reduction of the potentially devastating impact of urinary incontinence on an individual patients' quality of life. In this review, we explore the current theories on the mechanisms behind urinary incontinence.

Keywords Intrinsic sphincter deficiency; lower urinary tract; mixed urinary incontinence; overactive bladder syndrome; pathophysiology; stress urinary incontinence; urethral hypermobility; urgency urinary incontinence; urinary incontinence

Introduction

The lower urinary tract (LUT), consisting of bladder, urethra and urethral sphincter, has a dual function: storage and elimination of urine. Loss of the ability of the LUT to exert these functions can lead to debilitating functional disorders. Urinary incontinence (UI) is defined as 'the complaint of involuntary loss of urine'.[1] This devastating and often stigmatizing condition affects millions of people worldwide, the vast majority of whom are women (at least 2:1 ratio to men).[2] Prevalence estimates range from 5% to 69% in community-dwelling women, with most studies reporting a prevalence in the range of 25–45%.[2] Approximately 10% of all adult women report urine leakage at least weekly, with 25–45% reporting occasional leakage.[2] However, perhaps because of the associated stigma in some communities, or because it is still very often considered to be 'normal', UI is associated with low rates of presentation for care, which may lead to an underestimation of its true prevalence.

Of the UI subtypes, stress urinary incontinence (SUI) is the most common type of UI in women (49%). Thirty-four per cent of women with UI suffer from mixed urinary incontinence (MUI) and 15% from urgency urinary incontinence (UUI).[2] The other forms of UI, such as continuous UI or unconscious UI, are much less common. Men may also suffer from UI, typically after prostate surgery, or as a consequence of longstanding subclinical bladder outlet obstruction or chronic urinary retention (overflow UI). The prevalence of UI in men ranges from 1% to 39%, and, in contrast to women, UUI is the most predominant subtype (40–80%), followed by MUI (10–30%) and SUI (<10%).[2]

The presence of UI can lead to significant deterioration of a person's health, both physical and mental, and can thereby compromise an individual's ability to work and can even induce social isolation. However, the severity of UI is a poor predictor of UI-specific quality of life impairment. Therefore, both the severity of symptoms and the perceived bother and impact on activities of the symptoms have to be assessed in patients presenting with UI. Specific questionnaires have been designed to measure these factors simultaneously and prevalence estimates should take the degree of bother into account to allow measuring the true impact of this debilitating condition. UI also puts an enormous burden on healthcare cost, which, combined with its detrimental effect on the ability of some patients to work, leads to a huge economic impact on society, comparable to other chronic conditions such as ischemic heart disease or diabetes mellitus.

A wide variety of conservative (e.g. pelvic floor muscle therapy), medical (e.g. bladder relaxants), minimally invasive procedures (e.g. sacral neuromodulation) or surgical interventions (e.g. mid-urethral slings) are available to treat most types of UI, with efficacy rates exceeding 80%. However, the bladder has been called 'an unreliable witness'[3] and treatment efficacy relies heavily on identifying the correct underlying mechanism causing UI as soon as possible. Baseline tests in the workup of UI are validated questionnaires, urine dipstick, bladder diaries and uroflowmetry. Urinary incontinence may also be a manifestation of another underlying urological condition such as a urinary tract infection, stone disease or a tumour, and the presence of these should be excluded as a part of the diagnostic workup. Should the cause remain unclear and should first-line treatment options fail, then more invasive pressure-flow studies (urodynamics) may be indicated.

Understanding the pathophysiological mechanisms of the different types of UI is key to successful treatment and to reducing the condition's significant impact on the individual patient and on society as a whole.

Lower urinary tract function

The LUT consists of the urinary bladder, the urethra and the internal and external urethral sphincters (IUS and EUS). For the majority of time (>99%) the LUT exerts its main function: *storage* of the urine incessantly produced by the kidneys (the filling phase), allowing us to live our daily lives without continuously passing urine or becoming 'incontinent'. To permit this storage function of the LUT, a few conditions must be met. First, it is imperative that the urinary bladder can accommodate an

Michel Wyndaele *MD PhD FEBU is the Senior Clinical Fellow in Female and Functional Urology at Bristol Urological Institute, Southmead Hospital, Bristol, UK. Conflict of interest: none declared.*

Hashim Hashim *MBBS MRCS (Eng) MD FEBU FRCS(Urol) is Consultant Urological Surgeon and Director of the Urodynamic Unit at Bristol Urological Institute, Southmead Hospital, Bristol, UK. Conflict of interest: Dr Hashim Hashim is or has been an investigator, lecturer and consultant for pharmaceutical companies producing or developing drugs for lower urinary tract symptoms.*

Please cite this article in press as: Wyndaele M, Hashim H, Pathophysiology of urinary incontinence, Surgery (2017), http://dx.doi.org/10.1016/j.mpsur.2017.03.002

increase in volume without a significant pressure rise. This factor is called 'compliance', and is in normal conditions made possible by the elastic properties of the bladder wall. The urinary bladder consists of smooth muscle, the detrusor, which has the property to maintain a constant low tension over a wide range of stretch induced by the increase in volume during filling. The second necessary condition is an intact central and peripheral nervous system which suppresses the bladder smooth muscle during filling, prohibiting premature or unwanted bladder contractions. The final requirement is a closed outlet of the bladder: the IUS or bladder neck needs to maintain a high pressure and the EUS exerts a tonic tension with the ability to voluntarily contract in times of need (e.g. when there is an urge to void). The combination of a relaxed, compliant bladder with low pressure during filling and a high outlet pressure in bladder neck and EUS results in a pressure gradient which permits the storage of urine without leakage, or incontinence.

Information about the filling status is continuously sent to the central nervous system and at certain thresholds this information is passed on to the cerebrum to make us aware of the amount of urine in the bladder, eliciting either a first sensation of filling, a desire to void or a strong desire to void. This allows us to control and choose when the LUT exerts its second function: elimination of the stored urine (voiding phase). In normal circumstances, and in cognitively able persons, this will be done at a socially and emotionally appropriate time and location. Should voiding be wanted and appropriate, the central inhibition of the micturition reflex is lifted, inducing a detrusor contraction, and the pressure in the bladder neck and the tonic contraction of the EUS cease, resulting in a decrease in outlet pressure, initiating a reversal of the pressure gradient and evacuation of urine.

Lower urinary tract innervation

The normal function of the LUT is controlled by complex neural circuits in the spinal cord and brain that coordinate the activity of autonomic visceral smooth muscles in the urinary bladder and urethra with the activity of voluntary striated muscles in the EUS. These circuits act as on-off switches to shift the LUT between its two modes of operation, storage and voiding. This is unlike the more tonic patterns of activity of the autonomic pathways that regulate cardiovascular organs. Unlike many other visceral functions, micturition is under voluntary control and depends upon learned behaviour that develops during maturation of the nervous system. Disruption of (one of) these complex neuronal networks, or of (the actions of) their neurotransmitters, may lead to UI. A good knowledge of the innervation of the LUT may also dictate therapeutic choices for certain types of UI or development thereof.

Spinal and peripheral innervation (Table 1)

The LUT is peripherally innervated by three different nervous systems, which all contain both afferent sensory (both unmyelinated C-fibres and myelinated A-δ fibres) and efferent motor (mostly myelinated) nerves. The sympathetic autonomous nervous system innervates the bladder and bladder neck from spinal segments T10–L2 through the hypogastric nerve. The parasympathetic autonomous nervous system innervates the bladder and bladder neck from spinal segments S2–S4 through the pelvic nerve. Finally, the somatic nervous system innervates the pelvic floor, EUS and distal urethra from Onuf's nucleus in spinal segments S2–S4 through the pudendal nerve. Due to its anatomy, it is very susceptible to damage during labour or by sustained or repeated straining. The somatic nervous system provides the voluntary control of the EUS. Damage to the pudendal nerve may therefore directly lead to UI due to loss of control of the EUS. Women are more susceptible to this form of UI, as they have a weaker bladder neck and the EUS is their main sphincteric mechanism. To coordinate the activity of the smooth muscles of the LUT with the sphincteric striated muscles, integration of the autonomic and somatic efferent mechanisms within the lumbosacral spinal cord is necessary.

Central innervation

Coordination of reflexes and normal functioning of the urinary bladder not only occur through complex mechanisms in the spinal cord, but also involve supraspinal neural pathways, as conscious control of when to hold and when to evacuate is necessary in maintaining urinary continence. Axons of the neurons in the spinal cord receiving afferent input from the pelvis project to the brainstem, to the hypothalamus and, through relay neurons, to the cerebral cortex.

Lower urinary tract reflexes

Storage reflexes: during the storage of urine, distension of the bladder produces low level vesical afferent firing in the pelvic nerve, which in turn stimulates sympathetic outflow to the bladder and the bladder outlet (bladder neck and urethra)

Spinal and peripheral innervation of the lower urinary tract and its function

Nervous system	Spinal innervation	Peripheral innervation	Targets	Motor function	
				Filling	Voiding
Sympathetic autonomic nervous system	T10 – L2	Hypogastric nerve	Bladder neck	Contraction	
			Detrusor	Relaxation	
Parasympathetic autonomic nervous system	S2 – S4	Pelvic nerve	Bladder neck		Relaxation
			Detrusor		Contraction
Somatic nervous system	S2 – S4	Pudendal nerve	EUS	Tone + contraction	Relaxation

EUS = External urethral sphincter.

Table 1

Please cite this article in press as: Wyndaele M, Hashim H, Pathophysiology of urinary incontinence, Surgery (2017), http://dx.doi.org/10.1016/j.mpsur.2017.03.002