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Background, Etiology, and Subtypes of Urinary Incontinence

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Abstract: Urinary incontinence (UI) is the involuntary loss of urine. UI is a prevalent condition that affects people of all ages, becoming more common with older age, and which negatively affects the lives of millions of people. Although the pathophysiology behind UI is still being researched, we review here the basic neuromuscular system regulating urinary control and several other potential factors influencing the lower urinary tract dysfunction that contributes to UI including the urobiome and genetic variants. The specific subtypes, risk factors and findings associated with UI are reviewed.

Key words: urinary incontinence, urogynecology, overactive bladder, stress incontinence, neurogenic bladder, mixed incontinence

Background

Urinary incontinence (UI), defined as the symptom of involuntary loss of urine,[1] is a bothersome condition that negatively impacts the lives of millions of women. UI is estimated to affect up to 40% of adult women in the United States with prevalence increasing with age.[2,3] UI carries a large economic cost,[4] at a value comparable to costs of gynecologic/breast cancer or Parkinson disease, and is a major health burden that diminishes quality of life by negatively impacting daily living, physical activity, social relationships, sexual function, independence, and emotional well-being.[5]

UI can vary in degree of severity from rare and relatively nonbothersome symptoms of occasional small leakages to severe cases of complete bladder emptying occurring multiple times a day and night. Patients with UI often experience other lower urinary tract symptoms or LUTS. LUTS that may be seen in patients with UI include bladder storage symptoms (frequency, nocturia, urgency), sensory symptoms (increased, reduced, or absent bladder sensation) as well as voiding symptoms (such as hesitancy, intermittency, slow urinary stream, straining

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for urinating, and a feeling of incomplete emptying).[1]

Although highly prevalent in the population, UI and LUTS are frequently unrecognized and unaddressed leading to an underutilization of and delay in treatment and care. Patients are often hesitant to seek care and may not actively discuss their symptoms with their physician. Thus, it is of utmost importance to try to bring these symptoms into the open through standard intake questions and in direct conversations with patients.[6]

Most of the time UI can be diagnosed simply by history and treatment can be initiated without a subspecialty referral. Once we identify that a patient has bothersome UI, we can assess goals of care and review initial treatment options. Although not usually life-threatening, UI threatens quality of life and should be addressed with that in mind. In women who report UI, a urinary tract infection should be ruled out as this can be a contributory factor and, if present, once the infection is treated UI symptoms should be reassessed.[6] For more complex patients referral to a specialist or subspecialty provider may be necessary and can improve access to additional treatment options and evaluations. For primary care providers, the main task is to ask and create an open environment where patients can feel comfortable discussing their symptoms so that we can identify UI and help ensure access to appropriate care.

Neuromuscular Control of Urine

The controlled storage and release of urine is a multifactorial process involving proper coordination and functioning of a complex neuromuscular system that extends from the central nervous system to the bladder, urethra, and pelvic floor. To have a complete framework for understanding the etiology and different subtypes of UI, we will briefly review the anatomy and organization of the nervous system components involved in urinary storage and release.[7,8]

Control of the detrusor and urethral sphincter muscles is accomplished through signals passed from the central nervous system (comprised of the brain and spinal cord including the preganglionic neurons located in the lumbar spine) to the peripheral nervous system to control skeletal (urethral) and smooth (urethral and detrusor) muscle.

Within the central nervous system (CNS), brain imaging studies reveal that control of micturition involves the thalamus, the insula, the prefrontal cortex, the anterior cingulate, the periaqueductal gray (PAG), the pons [through the pontine micturition center (PMC)], the medulla and the supplementary motor area. The PMC is believed to set the volume at which voiding is triggered, but the PAG oversees the PMC to enable voluntary control (ie, you receive message to void from PMC but PAG enables you to wait until it is socially acceptable to empty your bladder) as it receives input from higher brain structures and is the primary input to the PMC.

Within the PNS, proper control requires the coordination of 2 systems that together regulate bladder function and sensation.

(1) The somatic system is responsible for mediating conscious or voluntary control of various bodily functions (such as voiding) through skeletal muscle contraction/relaxation and achieves urinary control through Onuf's nucleus and the pudendal nerve in order to prevent urinary flow through the urethra by contracting the striated muscle of the urethral sphincter.

    The pudendal nerve originates in Onuf's Nucleus (primarily located at S2), exits at S2 to 4, and releases acetylcholine to activate nicotinic receptors within the external urethral

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sphincter causing it to contract and obstruct urinary flow through the urethra.

(2) The autonomic system is responsible for mediating unconscious or involuntary control through smooth muscle. This control is accomplished within two subdivisions through which signals are transduced through autonomic ganglia connecting myelinated cholinergic preganglionic fibers and postganglionic fibers:

The sympathetic nervous system ("fight or flight") mediates urinary control through the hypogastric nerve in order to encourage urine storage (ie, people do not want to urinate and leave a scent when in "flight" from a predator).

- The hypogastric nerve, which originates from T11 to L2, releases noradrenalin from postganglionic fibers to stimulate beta-adrenergic (beta-3) receptors in the bladder (causing relaxation of the bladder detrusor muscle) and alpha (alpha-1) receptors in the urethra (causing contraction of the urethral smooth muscle).

Parasympathetic nervous system ("rest and digest") mediates urinary control through the pelvic nerve in order to stimulate urinary release or micturition and also regulates release of nitrous oxide to cause relaxation of the urethral sphincter (ie, when relaxed and safe you can then empty your bladder).

- The pelvic nerve, which originates from S2 to 4, releases acetylcholine from postganglionic fibers to stimulate muscarinic (mainly M3 with some M2) receptors in the bladder and cause contraction of the detrusor muscle.

  As part of this peripheral system, the pelvic nerves specifically act to coordinate the inhibition of parasympathetic output and stimulation of the striated urethral sphincter muscles as part of the "guarding reflex."

Sensory input: the pudendal, hypogastric and pelvic nerves carry sensory information from the bladder and urethra to the CNS through afferent lightly myelinated (a-delta fibers) and unmyelinated (C-fibers) nerves:

- The A-delta fibers react to distension and contraction and relay information regarding bladder filling through the pelvic and hypogastric nerves.
- The C-fibers are stimulated mostly by chemicals or cooling in the bladder and are thought to potentially play a role in irritative bladder symptoms and bladder pain conditions.

ETIOLOGY

UI can result from one isolated injury or many points of dysfunction within this system and can be worsened or even caused by outside factors that lead to increased urine production and inhibit proper bladder function. Often times, multiple causes or contributing factors can be identified for a patient affected by UI. This finding can be positive in that it enables the provider to create a multipronged approach to therapeutic improvement by addressing several contributing factors to gain improvement in overall bladder function.

Although we still do not completely understand the specific pathophysiology behind many types of UI, over the past few decades our understanding of potential contributors to the development of UI has significantly advanced. Many revolutionary treatment options have been discovered which have helped to further elucidate some of the mechanisms behind lower urinary tract dysfunction. There is still much to be learned about what causes

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UI, how to best treat UI, and ultimately how to prevent UI.

Neurogenic Dysfunction

There is a strong link between neurological injury and bladder dysfunction with bladder control issues frequently occurring after spinal cord injuries, stroke, and in conjunction with neurological disease such as multiple sclerosis, Parkinson disease, and even dementia.[7–9]

- Suprapontine lesions (eg, Parkinson or anterior cerebral lesions) remove inhibitory control of the PMC leading to detrusor overactivity and decreased bladder capacity.
- Spinal cord injury above the lumbosacral level initially results in an initial phase of spinal shock manifesting as a neurogenic acontractile detrusor and complete retention, with subsequent development of neurogenic detrusor overactivity and automatic micturition through spinal reflex pathways. This type of injury also carries a potential risk of detrusor-sphincter dyssynergia (contraction of detrusor with concomitant involuntary urethral sphincter striated muscle contraction) leading to incomplete emptying and possibly ureteral reflux.
- Spinal cord injury at the sacral level (eg, cauda equina) will often result in decreased detrusor contractility or the detrusor becoming acontractile, usually with impaired sphincter activity leading to retention, urinary stasis and an increased risk of urinary tract infection as well as potential for UI because of incomplete bladder emptying.

Role of the Genitourinary Microbiome

The recent discovery of a urinary microbiome (microbial communities that exist in the urinary tract, aka the urobiome) has been a major scientific breakthrough in our understanding of lower urinary tract physiology. A flurry of research has begun to uncover correlations that exist between the presence or absence of certain bacteria in the urinary system and the presence or absence of LUTS and UI. Preliminary studies have found evidence to support the existence of distinct differences between the gut microbiome and the urobiome within women and potential links between LUTS/UI and the following within the female urobiome[10,11]:

- Increased bacteria.
- Increased bacterial diversity.
- Presence/absence of specific *Lactobacillus* (eg, increased *Lactobacillus gasserei* and *Lactobacillus acidophilus*, and decreased *Lactobacillus crispatus*).
- Presence/absence of *Proteus* genus.
- Increased *Gardnerella.*
- Presence of *Actinobacteria* phylum (specifically *Atopobium vaginae* and *Finegoldia magna*).

Genetics

The search for a genetic link to the development of UI has been explored and recent advances in genetics as well as increased availability of genetic samples has increased our ability to test for this potential link. A recent systematic review examined evidence linking UI and various genetic variants. The review examined data from both animal and human studies which provided evidence showing that changes in specific signal transduction pathways and increases in inflammatory responses (specifically nerve growth factor) are associated with UI and increased bladder contractility.[12] Another recent study utilizing data from the Nurses' Health Study participants to search for genetic variants associated with UI and fecal incontinence found some exciting candidate variations that could provide a link to development of UI in women.[13] The authors of this study were

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able to identify 8 single nucleotide polymorphisms significantly associated with UI that were located within 2 loci (chromosomes 8q23.3 and 1p32.3) and they concluded that these preliminary findings support the existence of genetic associations for UI with further research needed.

Comorbidities/Risk Factors

UI has many risk factors and often the specific risk factor is associated with a specific type of UI. In the next section, we will review the various subtypes of UI and note various risk factors shown to be associated with that specific UI subtype. While there are specific associations, we have also included a nonexhaustive list of some of the more common risk factors or characteristics associated with the development of UI:

- Diabetes.
- Functional limitations (eg, limited mobility causing inability to walk to bathroom).
- Obesity/sedentary lifestyle.
- Cognitive limitations/dementia.
- Obstructive sleep apnea.
- Diuretic use.
- Constipation/bowel issues.
- Anatomic conditions (eg, urethral diverticulum, vesicovaginal fistula, etc.).
- Parity and mode of delivery (eg, spontaneous vaginal or operative vaginal delivery).

SUBTYPES

There are several subtypes of UI and we will utilize the definitions from the International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction.[1] This document specifically delineates the symptoms characterizing the various subtypes and also provides information on and definitions of signs and symptoms for other lower urinary tract, prolapse, anorectal, and sexual dysfunction conditions:

- Urgency urinary incontinence (UUI) is defined as the complaint of involuntary loss of urine associated with urgency (a sudden, compelling desire to pass urine that is difficult to defer). UUI commonly occurs in the setting of overactive bladder syndrome (OAB, urinary urgency with possible frequency, nocturia and/or UUI in the absence of other obvious pathology). UUI is particularly common with increasing age and is also associated with increased body mass index/weight, diabetes, use of diuretics, constipation, and functional limitations. On urodynamic assessment patients with UUI can show detrusor overactivity, decreased bladder capacity and increased bladder sensation (ie, they feel full at lower volumes than normal controls). Bladder diaries in these women will often show frequent low volume voids and a decreased capacity with possible nocturia and UUI episodes noting common triggers such as washing dishes with warm water, standing up from a period of sitting, and putting the key in the door upon getting home.
- Stress incontinence (SUI) is defined as the complaint of involuntary loss of urine on effort or with physical exertion (eg, exercising, coughing or sneezing). SUI is the most common type of UI and usually starts to become bothersome and significantly affect women in their 40 to 50s. SUI is associated with obesity, prior vaginal delivery, and prior operative vaginal delivery, and is thought to be a result of weakening in the urethral sphincter tone/strength, which decreases urethral resistance and makes it easier for urine to pass with intermittent increases in abdominal pressure.[14,15] SUI can be observed on physical exam through a positive cough stress test in the office as well as during urodynamic assessment, and

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patients may demonstrate a reduced mean urethral closure pressure on urethral pressure profile urodynamic studies. Bladder diaries show relatively normal bladder function except for leakages noted with exercise, cough, sneezing, and exertion (eg, lifting a heavy box).

- Mixed incontinence (MUI) is defined as the complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing. In other words, MUI is the presence of both SUI and UUI in an individual patient, and thus carries similar risk factors to as UUI and SUI, noting that the presence of SUI or UUI increases the risk for subsequent development of MUI.[16] MUI is often described based on the more bothersome or dominant subtype (ie, urge predominant or stress predominant) and this distinction or recognition of the more bothersome type of UI can help guide the therapeutic approach.
- Adult neurogenic lower urinary tract dysfunction (ANLUTD) is the new recommended term for conditions that were previously grouped into neurogenic bladder.[9] ANLUTD is only diagnosed in the presence of a known relevant neurological disease, and in so doing, encompasses UI and LUTD in the setting of neurological conditions that affect urinary function through the CNS, PNS, detrusor, and/or urethra in women.
- Nocturnal enuresis (NE) is defined as the complaint of involuntary loss of urine that occurs while sleeping. This can be without an urge to void with patients noting the void after waking up wet. Nocturnal enuresis can also be seen in the presence of OAB or nocturnal polyuria (over 20% to 30% of 24 h urine output produced at night when patient is sleeping) or with various sleep disorders, most commonly obstructive sleep apnea, which can contribute to the development of NE because in disrupting the normal sleep cycle, the body may increase atrial natriuretic peptide leading to nocturnal diuresis. NE commonly occurs with other LUTS, so risk factors for NE are similar and include obesity, smoking, hypertension, and a sedentary lifestyle, with additionally a higher prevalence of NE seen in patients with hemoglobinopathies.[17]
- Postural incontinence is defined as the complaint of involuntary urinary loss with a change in body position and can occur in the setting of either UUI or SUI.
- Continuous incontinence is defined as the complaint of continuous loss of urine involuntarily. Continuous incontinence should trigger an evaluation for anatomic abnormality, particularly the presence of a fistula, to determine the source of continuous urinary leakage.
- Insensible incontinence is defined as the complaint of UI when the patient is unaware of how the UI occurred. Insensible incontinence can be because of cognitive dysfunction as well as potential neurological dysfunction altering sensory signals and the ability to sense urge, leakage, etc. When in the setting of impaired cognition, this type of UI should be referred to as impaired cognition urinary incontinence.
- Coital incontinence (CUI) is defined as the complaint of involuntary loss of urine during sexual intercourse and can occur at various times (upon penetration, during intercourse, at orgasm, or a combination) or with certain sexual positions. In women with UI, CUI is common, and the specific type of CUI may correlate with the subtype of UI. For example, women with SUI are more likely to have CUI at penetration (likely because of increased bladder pressure from penetration leading to leakage), and women with UUI or urge

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predominant MUI are more likely to have CUI at orgasm (likely because of detrusor contraction occurring during orgasm).[18]

- Another subtype of UI that bears mentioning is UI resulting from impaired mobility or mobility limitations, which implies that the incontinence occurs because of the presence of a disability that prevents the patient from getting to the bathroom on time. This type of UI can often affect patients with OAB who then, upon having more limited mobility, experience the onset of or worsening of UUI symptoms.

Summary

As we have reviewed here, there are many subtypes of UI and our understanding of the relationship between subtypes as well as the specific causes, definitions, and etiologies of each is constantly evolving as we gain further insight into the physiological mechanisms regulating urinary control. First and foremost, our primary task as health care providers is recognition of UI by asking questions and screening for symptoms, so that we can identify and provide treatment for the millions of women affected by these burdensome conditions.

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