Stress urinary incontinence (SUI) is the involuntary loss of urine with activities that increase intra-abdominal pressure, such as coughing, sneezing, and walking. Treatment options vary and include behavioral modifications, pelvic floor muscle exercises (PFMEs), barrier methods, bulking agents, and surgery. No drug approved by the Food and Drug Administration (FDA) exists for SUI. A few agents are occasionally used off label for SUI, but randomized controlled trials proving their efficacy and safety for this indication are lacking.

Urinary incontinence (UI) of any type is an important health concern that often has a substantial effect on an individual’s perception of well-being, body image, and quality of life (QOL). It is estimated that 13 million people in the United States, of which 11 million are women, suffer from UI (1). The actual prevalence of UI in women is not known. Most women who experience UI never seek or receive treatment (2,3). A limitation of existing national databases is that they capture only the minority of incontinent women who are treated for incontinence.

The economic impact of UI is better understood and formidable. According to the recently published Urologic Diseases in America Project, UI in women was the chief reason for more than 1 million office visits in the year 2000 at a cost of $452 million (4). Despite the public’s recognition of the disorder, embarrassment and fear that surgery is the only treatment option can still inhibit a woman from discussing incontinence with her physician. A prodigious growth of information and treatment options for UI has developed, but SUI remains without an effective pharmacological treatment.
ANATOMIC AND FUNCTIONAL INFLUENCES ON CONTINENCE

Female continence is maintained by the interplay of several anatomic and functional mechanisms. With increases in intraabdominal pressure, the abdominal pressure is passively transmitted to the proximal urethra, followed by active contraction of the striated external sphincter. The suburethral supportive layer of periurethral fascia, anterior vaginal wall, and levator ani muscles act as a backboard of support against which the urethra is compressed during increases in intraabdominal pressure so that leakage does not occur. Also contributing to continence is reflex contraction of the levator muscles that directly increases midurethral pressure. Addition of voluntary contractions of levator and obturator muscles to increase tension on the urethropelvic ligaments does the same. Alteration or damage to any of these anatomic structures may result in SUI, and anti-incontinence surgery attempts to restore the anatomic deficits contributing to leakage.

However, prevailing theories of continence hold that the etiology of SUI is not purely anatomic. Functional factors such as the intrinsic urethral function are responsible as well, a concept illustrated by the observation that not all women with hypermobility of the urethrovaginal unit leak. The intrinsic function of the urethra is related to its makeup of smooth and striated muscle, connective tissue, vascular plexus, and mucosa, which together provide inwardly directed forces that help coaptation and, ultimately, continence.

Nervous system control of the lower urinary tract is another integral part of its physiology and the pathophysiology of incontinence. It plays a crucial role in determining the detrusor capacity and compliance as well as urethral competence necessary to maintain or restore continence. Extrinsic efferent innervation of the lower urinary tract includes three major nerves carrying the three principal divisions of the peripheral nervous system: sympathetic, parasympathetic, and somatic. Activity of the detrusor smooth muscle, bladder neck muscles, and internal sphincter are autonomically controlled, whereas the striated muscle of the external sphincter is controlled by the somatic branch of the peripheral nervous system (5).

The autonomic nervous system predominates in the lower urinary tract. The hypogastric nerve carries sympathetic input responsible for bladder relaxation and exerts its effect through β-adrenergic receptors (β₂) at the detrusor and α₁- (α₁) receptors in the bladder neck and proximal urethra. The pelvic nerve carries parasympathetic input for bladder contraction via acetylcholine stimulation of muscarinic receptors (M3) in the body of the detrusor. The distribution of autonomic receptors in the lower urinary tract varies. Numerous types of postsynaptic nerve receptors exist: α-adrenergic, β-adrenergic, cholinergic, histaminic, and serotonergic. In general, β-adrenergic stimulation produces smooth muscle relaxation, and α-adrenergic and cholinergic stimulation cause muscle contraction.

Specific receptor functions at specific lower urinary tract sites are still incompletely understood. The detrusor is predominantly supplied with postganglionic parasympathetic cholinergic nerve terminals. Few noradrenergic nerves targeting β-adrenergic receptors are found at the trigone and none in the detrusor. The β-adrenergic receptors in the detrusor facilitate relaxation and bladder filling. Cholinergic receptors in the dome are responsible for detrusor contraction during micturition. The α-adrenergic receptors of the α₁-subtype are found in low density in the detrusor, and other α-adrenoceptors are absent. Newly recognized serotonin (5-HT) receptors within the detrusor appear to facilitate neuromuscular cholinergic transmission (6). H₁ histamine receptors have also been identified in the detrusor, but currently no role for histamine as a neurotransmitter in the lower urinary tract has been discovered (7).