Overactive Bladder in Children. Part 1: Pathophysiology

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Purpose: Detrusor overactivity is the most common voiding dysfunction in children. Detrusor overactivity is also known as overactive bladder syndrome, urge syndrome, hyperactive bladder syndrome, persistent infantile bladder and detrusor hypertonia. It has become apparent that the ideas that had been used to dictate the management of this problem in children were based on the foundation that this is a primary bladder problem and/or a delay in maturation in the nervous system of children. The expectation that children would outgrow the problems led many pediatric urologists and other practitioners to tell the parents of these children that they would not be wetting themselves on their wedding day. It has become apparent from recent studies in adults with voiding dysfunction that they had symptoms present as children. The recent findings of associations with lower urinary tract symptoms and sexual dysfunction, and the association of voiding dysfunction and neuropsychiatric problems has opened up a new frontier into the possible mechanisms of overactive bladder syndrome in children that would explain these problems, tie them together and explain the continued problems that adults face. These findings point to overactive bladder syndrome as a symptom of a more centrally located dysfunction that affects multiple systems, notably bowels, bladder, sexual and ejaculatory function, control of blood pressure, and even mood and behavior.

Materials and Methods: We looked at the neuroanatomy, neurophysiology and neuropharmacology of voiding. Available research and clinical data in the urological field as well as outside of the field were combined to generate a unified theory that could possibly explain many associated symptoms that are commonly found in pediatric overactive bladder syndrome.

Results: The available data indicate that pediatric overactive bladder syndrome and many pediatric voiding dysfunctions may be part of a more generalized problem that affects multiple systems, notably bowels, bladder, sexual and ejaculatory function, control of blood pressure, and even mood and behavior. We explained the relationship that the bowel has with pediatric overactive bladder syndrome and also the link that other neuropsychiatric problems have with overactive bladder syndrome.

Conclusions: The movement away from a vesicocentric way of thinking to a more corticocentric mode of thinking along with new imaging modalities that can look at the brain and examine it as it works will be of great value for determining future treatments. Medications generated from these evidence based studies will hopefully treat the underlying disease process and not just the symptoms.

Key Words: bladder; urinary bladder, overactive; physiopathology; brain; neurophysiology

Detrusor overactivity is the most common voiding dysfunction in children. Detrusor overactivity is also known as OAB, urge syndrome, hyperactive bladder syndrome, persistent infantile bladder and detrusor hypertonia. Its onset can be slow and insidious with a gradual increase in the strength of the urge to void that can occur during a long period. It can also be quite sudden with dramatic episodes of incontinence in children who were normally dry in a brief period. Overactive bladder appears to have a peak incidence between ages 5 and 7 years. Ruarte and Quesada found an incidence of 57.4% in a group of 383 incontinent children who were 3 to 14 years old.[1] The group consisted of 38.9% boys and 60.1% girls. Enuresis is estimated to affect 5 to 7 million children in the United States 6 years or older. The impact of enuresis in children can be quite profound. It can affect life socially, emotionally and behaviorally, and it will also impact the everyday life of the family.[2] We know that urinary incontinence is a large problem with a total economic impact in the United States of $26.3 billion in 1995.[3,4] This is a quite significant economic burden on our society. From our understanding of overactive bladder we know that, if it continues for a long time, we see thickening of the bladder wall, which has an impact in adulthood. As patients become older, its consequences become more profound and require more of an effort to correct.[3,4] We have seen the overall cost of urinary incontinence management increase from $3.94 billion in 1984 to $19.5 billion in 2004.[5] The cost associated with the indirect consequences of urinary incontinence could even be higher. Problems include skin breakdown, the need for psychiatric care and treatment for urinary tract infections. These costs can amount to quite a significant amount, far in excess of the amount that is directly associated with OAB.

From a pediatric urologist perspective the child who has overactive bladder has a good chance of becoming an adult who continues to have problems with overactive bladder. This correlation was seen in 2 published reports. In the first study Fitzgerald et al noted that OAB in childhood correlated with adult OAB symptoms.[6] They found that frequent daytime voiding in childhood correlated with adult urgency. A correlation exists between childhood nocturia and adult

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nocturia. Childhood daytime incontinence and nocturnal enuresis were associated with a more than 2-fold increased association with adult urge incontinence. Also, a history of childhood urinary tract infections correlated with a history of adult urinary tract infections. In another study in 170 women Minassian et al found a higher prevalence of childhood voiding dysfunction in women who had urinary frequency, urgency, stress incontinence and urge incontinence.[7] They also noted a greater likelihood of a higher body mass index in their symptomatic patients.

The implications of these findings underscore the importance of childhood OAB and its impact in adulthood. The trend with time has been to tell parents that these problems are self-limiting and they will resolve in due time as the child matures. It appears that this may not be the case. As they mature, some children are better at compensating for the problems and they eventually drop off the radar screen (our offices) because of frustration with our inability to treat the problems or because they have coping strategies that satisfy their needs for the interim. A better understanding of the potential causes of childhood OAB could prevent undue problems in adulthood and make many children much happier along with their parents and teachers.

THE PREVAILING THOUGHTS ON PEDIATRIC OAB

Overactive bladder is not completely understood and the belief is that it most certainly is a multifactorial problem. In some instances anatomical abnormalities can lead to overactive bladder (these cases are not discussed in this review), while in other cases functional voiding problems may be the source of overactive bladder. In other instances neurological lesions may lead to the development of overactive bladder.

The prevailing theory in children is that overactive bladder is believed to be due to a delay in the acquisition of cortical inhibition over uninhibited detrusor contractions in the course of achieving the mature voiding pattern of adulthood. The site of maturational delay is thought to lie in reticulospinal pathways of the spinal cord or it could be in the inhibitory center in the cerebral cortex. We know that cortical control is normally established between ages 3 to 5 years. Delay in fine-tuning bladder sphincter coordination during voiding causes uninhibited detrusor contractions, to be met with voluntary external urethral sphincter contractions, of which the control is thought to be acquired at an earlier age.[8] An increase in intravesical pressure can manifest in an array of symptoms, including urgency, urge incontinence and nocturnal enuresis. Overactive bladder triggers bladder overactivity, usually in the early filling phase, causing the pelvic floor to respond by voluntary contraction. This voluntary contraction leads to classic holding maneuvers, such as leg crossing, penile grabbing and squatting. It is thought that active external sphincter contraction may possibly cause a temporary reflex relaxation in the detrusor, therefore, affording momentary relief from the effects of uninhibited bladder contractions. Persistent isometric contractions of the detrusor against the tightened sphincter or incomplete relaxation of the sphincter leads the bladder muscle to hypertrophy. This increased hypertrophy leads to a gradual decrease in functional bladder capacity and increased bladder instability, creating a vicious cycle by which overactive bladder is worsened. The concomitant increased pelvic floor activity may be associated with increased autonomic stimulation of the perineal organs and musculature. This increased activity may be associated with sexual dysfunction in adults.[9–13]

There is now compelling evidence that high pressure voiding occurs during gestation in the fetus. Investigators have made us aware that abnormal high pressure voiding during gestation may be the cause of renal damage in reflux (the water hammer effect).[14–21] This abnormal voiding may persist in some cases. The probable lack of outright detrusor abnormalities in these bladders would lead us to believe that the problem is more likely to originate from a neurological source. It is the contention of Mitchell that the lack of proper bladder cycling in the exstrophic bladder is the primary cause of why these bladders fail to function properly even after they have been closed.[22] A similar example exists with boys with posterior urethral valves. In this group even long after the valves have been ablated and bladder muscle has thinned out there are persistent abnormal voiding patterns. These situations are analogous to children with a tracheoesophageal fistula or tracheostomy who is not fed early in life, who generally fails to develop normal swallowing patterns and who requires intensive retraining. In all of these cases there appears to be a link between repetitive normal muscle activity and the development of normal voiding and swallowing mechanisms. This form of muscle memory is most likely imprinted in the brain during development and it is crucial to the proper functioning of the voiding reflexes during development and postnatally.

A finding that confirms a central process and a genetic mode of transmission for voiding dysfunction is the Ochoa urofacial syndrome.[23] In many ways the Ochoa syndrome is similar to the Hinman (nonneurogenic neurogenic bladder) syndrome. The Ochoa syndrome was first described by Ochoa from Colombia in 1979. Its prevalence is quite low and fewer than 200 cases have been reported. The syndrome is genetically determined and associated with an unusual inversion of facial expression when smiling is attempted. The face becomes contorted into a grimace that makes it appear as if the subject is sobbing and crying, thus, making it possible to recognize afflicted patients early in life. The Ochoa syndrome is characterized by hereditary transmission. The syndrome can be identified as early as age 2 years. There is a consistent relationship between the grimacing expression on the face and the dysfunctional voiding pattern. There is also a recessive pattern of inheritance. The micturition reflux is processed in the reticular formation of the brainstem in close anatomical proximity to the origin of the facial nerves. Lesions in the reticular formation are expected to produce functional lesions affecting coordination, rather than paretic lesions, as when the nuclei are involved. Given the proximity of this lesion to the facial nerves, we see that the facial expression is associated with this abnormality. Urofacial syndrome has been mapped in immunology laboratories at University of Florida using homozygosity mapping and DNA pooling strategies in families from Colombia. In 1997 the gene was mapped at chromosome region 10q23-4.[24] Subsequently genetic homogeneity was demonstrated through homozygosity mapping in American patients of Irish heritage. These examples may underscore the role of the central nervous system in the control of micturition. The fact that reflux is known to have a hereditary pattern and many children with OAB have parents with similar symptoms as well as data in this review point to the underlying cause of OAB as an inheritable problem.

PATHOPHYSIOLOGY OF OVERACTIVE BLADDER

Symptoms of hyperreflexia may have many potential causes and contributing factors. Urination involves the use of higher cortical centers in the brain, pons, spinal cord, peripheral autonomic somatic and sensory afferent receptors in the lower urinary tract as well as anatomical components of the lower urinary tract. Any disorder of these structures may contribute to symptoms of overactive bladder. The normal bladder functions like a compliant balloon filling gradually. In the compliant bladder as it fills, the pressure remains low. This decreased pressure is lower than the typical urethral resistance. With normal urination urethral resistance decreases and detrusor contraction empties the bladder. Detrusor overactivity is usually associated with involuntary detrusor contractions. Overactivity of the detrusor from neuropathic causes can result in urgency or urge incontinence depending on the response of the sphincter.

Overactive bladder may also have a myogenic origin. The prevailing theory for many years has been that myogenic abnormalities are a primary cause of overactive bladder. Treatment of these problems rests primarily on the use of anticholinergics that target muscarinic receptors. It would seem simplistic to think that there would be a primary myogenic problem that affects the bladder without some form of myogenic processes that would affect other smooth muscles. It would make more sense to implicate a process that causes detrusor hyperplasia due to neurological causes or outlet obstruction as the source of these myogenic problems. Eventual correction of these problems should be the mainstay of treatment. This approach would eventually treat the underlying problem and eradicate the symptoms instead of just concentrating on the symptoms, as we have for many years.

There are various efferent and afferent neural pathway reflexes, and central and peripheral neurotransmitters that are involved in urinary storage and bladder emptying. Their relationships as of yet are not completely understood. With functional magnetic resonance imaging and positron emission tomography we are starting now to see and understand better the role that these central neurotransmitters may have. Serotonergic activity facilitates urine storage by enhancing the sympathetic reflex pathway, inhibiting the parasympathetic voiding pathway. Dopaminergic pathways may exert inhibitory and facilitory effects on voiding. Dopamine Dl receptors appear to have a role in suppressing bladder activity, whereas dopamine D2 receptors appear to facilitate voiding. Other neurotransmitters, such as α-aminobutyric acid and enkephalin, inhibit voiding in animals. Acetylcholine, which interacts with muscarinic receptors at the detrusor, is the predominant peripheral neurotransmitter responsible for bladder contraction. Pathological states can alter sensitivity to muscarinic stimulation, for example bladder outflow obstruction appears to enhance responses to acetylcholine, similar to denervation supersensitivity. Normally only a small proportion of bladder contractions are resistant to atropine, probably as a result of the interaction of ATP with purinergic receptors. However, ATP may have a more prominent role in bladder contractions in patients with overactive bladder (fig. 1).[25]

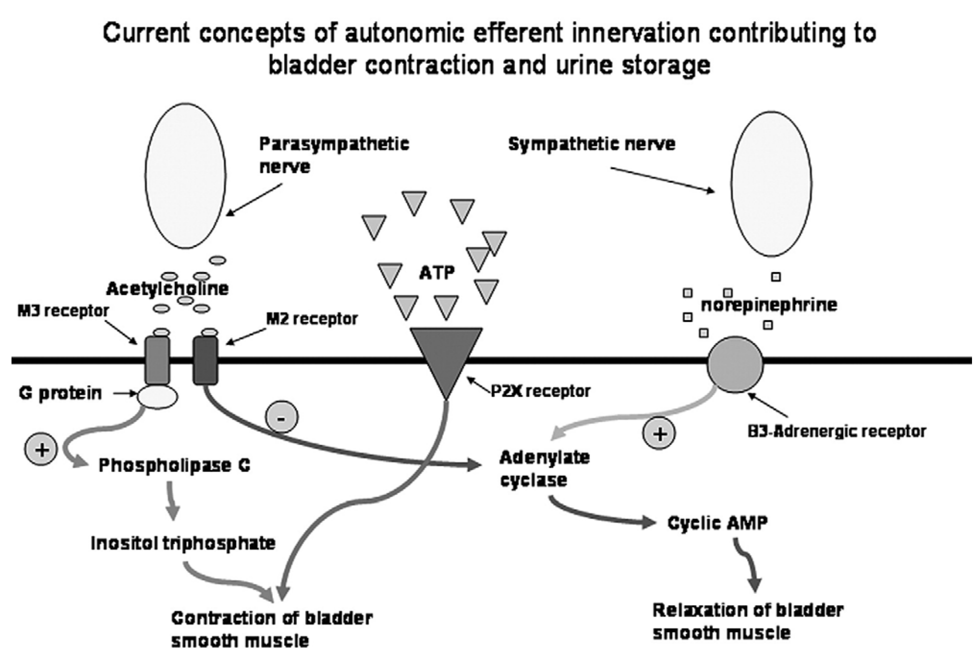

FIG. 1. In normal human bladder acetylcholine is predominant neurotransmitter that causes bladder contraction. Acetylcholine interacts with M3 and M2 receptors. M3 receptor activates phospholipase C through coupling with G proteins, which generates inositol triphosphate, which in turn causes calcium release from sarcoplasmic reticulum and bladder smooth muscle contraction. M2 receptors contribute to bladder contraction by inhibiting adenylate cyclase activity and decreasing cyclic adenosine monophosphate (*AMP*) levels intracellularly, mediating bladder relaxation. In normal human bladder only small proportion of bladder contraction is resistant to atropine. Resistance to atropine most likely is due to interaction of ATP and purinergic (*P2X*) receptors. Stimulation of β3-adrenergic receptors may also lead to bladder relaxation.[29] Plus sign indicates activation. Minus sign indicates inhibition.

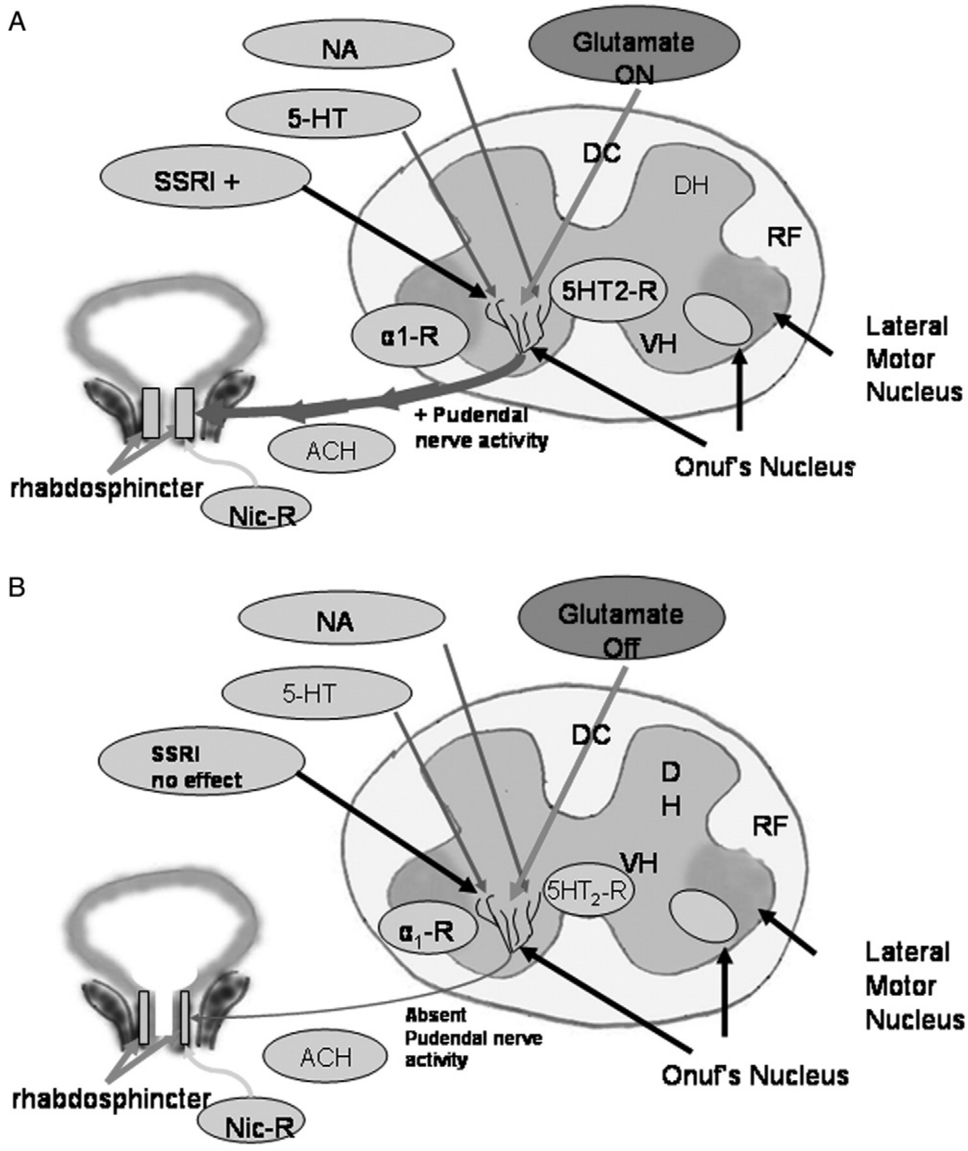

FIG. 2. *A*, storage phase. Selective 5-HT reuptake inhibitors (*SSRI*) are believed to increase 5-HT in sacral spinal cord so that, when glutamate signal is turned on during urine storage, increased pudendal nerve activity enhances rhabdosphincter contraction. *B*, voiding phase. When glutamate is turned off during voiding, pudendal nerve activity is eliminated and rhabdosphincter is relaxed even in presence of selective 5-HT reuptake inhibitors.[30] α_1*-R*, adrenergic receptor. *DC*, dorsal column. *DH*, dorsal horn. *NIC-R*, nicotinic receptor. *RF*, receptor field. VH, ventral horn. *5HT2-R*, 5-HT-2 receptor. *Onuf's nucleus*, Onufrowicz's nucleus. *ACH*, acetylcholine.

Anatomical correlates of detrusor overactivity have been described. The bladder of patients with detrusor overactivity appear to have abnormal gap junctions between smooth muscle cells. Such further correlates require further study. Increasing attention has been paid to the lower sensory afferent nerves in normal voiding and overactive bladder.[25] During bladder filling afferent activity of the bladder and urethra reaches the spinal cord, predominantly via the pelvic nerve. Sensory input during bladder filling results in an increase in sympathetic tone. NA release from the hypogastric nerve stimulates β3-adrenergic receptors in the bladder to cause the smooth muscle to relax as well as α-adrenoceptors in the smooth muscle of the bladder neck and proximal urethra to contract. Acetylcholine released by the somatic pudendal nerve and sacral nerve fibers elicits contraction of the striated urethral sphincter and pelvic floor.

Glutamate is thought to be the primary descending neurotransmitter for the storage reflex. Glutamate is released in the ventral horn of the sacral spinal cord (Onufrowicz's nucleus). In Onufrowicz's nucleus axons projecting from the central nervous system synapse with the pudendal nerve. The release of glutamate activates the pudendal nerve and leads to contraction of the rhabdosphincter. It should be noted that Onufrowicz's nucleus is densely populated with 5-HT and NA terminals, and contains a high density of 5-HT and NA receptors. NA and 5-HT have a modulatory role, in that they enhance rhabdosphincter contraction but are not able to induce rhabdosphincter contraction on their own (fig. 2).[26] After micturition starts glutamate is no longer released and pudendal nerve activity ceases.

Myelinated A-δ sensory fibers respond to passive distention and active contraction of the detrusor muscle. Unmyelinated sensory C fibers have a higher mechanical threshold and respond to various neurotransmitters. C fibers are relatively inactive during normal voiding but they may have a critical role in overactive bladder symptoms in patients with neurological and other disorders. Several types of receptors have been identified in afferent nerves, including vanilloid receptors, which are activated by capsaicin and possibly by endogenous anadamide, purinergic receptors, which are activated by ATP, neurokinin receptors, which respond to substance P and neurokinin A, and nerve growth factor receptors. Other substances, including nitric oxide, calcitonin gene-related protein and brain derived neurotrophic factor, may also have an important role in modulating the sensory afferents in the human detrusor.[25] Better understanding of the complex interplay among these various neurotransmitters may yield new and more specific targets for drug treatment for overactive bladder. A full discussion of the role of all of the neurotransmitters involved in the urination process is beyond the scope of this review. An excellent review of these neurotransmitters and their functions is available in an article by Yoshimura and Chancellor.[27]

NEURAL PATHWAYS

The micturition center in the spinal cord is primarily located in 3 sacral spinal cord segments (S2–S4) with S3 the most important. This is anatomically located at vertebral levels T2 through L1. The gray matter in the spinal cord is divided into a series of zones. The parasympathetic preganglionic motor neurons lie within an intermediolateral gray column. The cells extend in a vertical plane along the border between the white and gray matters, and in a horizontal plane at the base of the dorsal horn at lamina 7 and lamina 5 in the dog. The former serves as the center for bladder control and the latter, more medial gray matter of parasympathetic cells serves as the rectal control. Somatic nerve fibers originate from the nucleus of Onufrowicz in the mid ventral spinal gray matter. Innervations to most striated muscles of the pelvic floor, including those of the periurethral and anal sphincters, originate in the nucleus of Onufrowicz. Activity travels up the spinal cord via the spinothalamic tracts. Exteroceptive signals carried up the spinothalamic tracts include sensations of pain, temperature and touch generated in the urothelium. Proprioceptive sensory impulses initiated in the bladder muscles and periurethral striated muscle travel in the posterior columns. Proprioceptive axons enter the dorsal portion of the gray matter, otherwise known as the periaqueductal gray area, and turn to travel rostral to synapse in the pontine mesencephalic reticular formation. Exteroceptive sensory impulses travel in the spinothalamic tracts and synapse in the thalamus and sensorimotor cortex.[28]

In humans stimulation of the hypogastric plexus originating from spinal levels T-10 through L-2 results in detrusor muscle relaxation and intrinsic sphincter contraction, thereby inhibiting micturition. Stimulation of passive sympathetic nerves originating from spinal level S-2 through S-4 has the opposite effect. In children a common procedure performed to cause the urge to urinate to cease is squeezing of the glans penis.[29] Clitoral compression can cause similar effects in girls. Studies have shown that this causes the cessation of intravesical pressure on urodynamics during the filling phase. The pudendal nerve reflex has been proposed as the mechanism of bladder inhibition with this maneuver. Squatting on the heel in girls and what appears to be masturbatory behavior in boys could actually be a mechanism used by some children to suppress bladder contractions. Pudendal nerve stimulation stimulates the sympathetic system that suppresses bladder activity via the β-adrenergic system with spinal interneurons that release inhibitory neurotransmitters, such as in enkephalin, glycerin and α-aminobutyric acid.

The role of 5-HT and NA in the nervous system is far ranging. In the enteric nervous system 5-HT predominates, while NA predominates in the sympathetic autonomic nervous system. Neurons expressing 5-HT and NA are concentrated in a few distinct nuclei in the brainstem, ie the medulla and pons, but these axons traverse large distances from the prefrontal cortex to the caudal spinal cord. These neurons are involved in the fight or flight reflex through facilitating motor activity and inhibiting pain perception. They have a major role in the regulation of mood, pain perception, attention, temperature, gastrointestinal motility, sleep, sexual function and the micturition process.[26] These neurotransmitter pathways appear to be gaining increasing importance in the management of voiding dysfunction in children and adults. Their ability to modulate critical functions appears to be the central role of these pathways. Most voiding dysfunctions that we see appear to be a problem of poor modulation of reflexes that are an all or none response. It is not surprising that agents that affect 5-HT and NA homeostasis have effects that are far ranging, from treatment of depression to lower urinary tract symptoms, and erectile and ejaculatory dysfunction.

It was initially thought that sacral neuromodulation was mainly effective in the pelvic floor muscles by inducing muscle hypertrophy. The change in histochemical properties was supposed to lead to improved pelvic floor efficiency. Because neuromodulation occurs below the threshold for direct motor responses, this theory is not convincing. Today it is well accepted that the effects of sacral root modulation occur at the spinal and supraspinal level by the inhibition of spinal tract neurons involved in the micturition reflex and interneurons involved in spinal segmental reflexes in postganglionic neurons. Furthermore, there may be inhibition with the primary afferent pathway and indirect suppression of guarding reflexes by turning off the bladder input to internal sphincter sympathetic or external urethral sphincter interneurons. Also, in urinary retention we achieve effects believed by some groups to be the result of changed pelvic floor behavior directly or as part of a returning brainstem on/off switch mechanism.[30]

Functional magnetic resonance imaging and positron emission tomography indicate that bladder fullness is associated with increased activity in the anterior mesencephalon.[31–34] Signals from there were seen to travel to the substantia nigra. This is a source of ascending dopaminergic neurons to the striatum, which is reciprocally connected to the brainstem micturition centers. The anterior mesencephalon was also seen to connect to the pons and medulla (micturition center) with increased activity. A third site of increased activity was noted in the cortical centers, primarily in the anterior and posterior cingulate gyrus. The anterior gyrus is associated with executive activity, while the posterior gyrus is associated with evaluative activities. An example of a typical evaluative activity would be the decision that is made to empty the bladder, although it is not completely full. This cognitive functioning would prevent a sudden urge to have to go to the bathroom. Patients who have increased activity in the micturition centers and mesencephalon with urgency typically do not have increased activity in the cortical centers, primarily the cingulate gyrus. In a group of patients who had urge syndrome with spinal stimulators after the stimulators were turned on increased activity in the cingulate gyrus areas was noted. The cingulate gyrus is associated with contextual representations, better known as behavior control. The inability to activate this cingulate gyrus and suppress autonomic activities leads to hyperreflexia.

Inactivity in the cingulate gyrus may be a good explanation for the overactive bladder seen in familial settings. This decreased activity in the cingulate gyrus and frontal lobes may also explain the high association of voiding dysfunction in patients with behavioral, learning and psychiatric disorders. Disorders such as Asperger's syndrome, Tourette's syndrome, bipolar disease, depression, obsessive compulsive disorder, panic disorders, anxiety disorders, attention deficit disorder and attention deficit hyperactivity disorder are associated with decreased frontal lobe activity.[35] It is well known that there is an increased incidence of urinary incontinence in children with attention deficit disorder/attention deficit hyperactivity disorder.[36, 37] It is also recognized that in children who have problems with incontinence the incidence of behavioral and psychiatric disorders is 3 times greater than in the general population.[38–40] An association exists between increased urinary incontinence and obesity.[41] There is also an increased association with stool incontinence and constipation in patients with obesity.[42] Recent studies indicate that there is an increased incidence of obsessive-compulsive behavior in chronically obese male and female patients as well as an increased incidence of depression in chronically obese males.[43] This association between obesity incontinence and constipation may be linked to a possible problem with disinhibition in the frontal lobe that can explain all 3 phenomena.

THE ROLE OF CONSTIPATION

There is a close association between constipation or fecal retention and overactive bladder. The mainstay in the management of overactive bladder is the correction of constipation and fecal retention. An understanding of normal defecation is essential for understanding problems associated with overactive bladder. The stimulus for defecation is initiated primarily by rectal distention. There are no other receptors in the rectum other than stretch receptors. The rectum normally distends when peristaltic activity propels feces from the sigmoid colon to the rectum, stimulating sensory receptors in the rectal wall. When picked up, these sensations are sent to the brain and processed as a sense of distention. Rectal distention causes involuntary temporary contraction of the striated external sphincter and puborectalis muscles. Voluntarily maintaining this contraction causes the rectum to adapt to the increased volume and the sense of fecal urgency subsequently disappears until the arrival of another fecal bolus. This mechanism lends itself easily for children to develop large, distended rectums with time as well as fecal hoarding and chronic pelvic floor hypertonicity. In a study Miyacato et al found that rectal distention leads to decreased amplitude and a shortened duration of bladder contraction, and finally it can almost abolish bladder activity.[44] These effects can be reversed by the injection of strychnine and bicuculline intrathecally. This restores the amplitudes of bladder contractions to control levels.

It is postulated that an inhibitory rectovesical reflex exists in the lumbosacral cord of rats. The afferent limb in the spinobulbospinal micturition reflex pathway may be additionally and redundantly inhibited by glycinergic and GABAergic mechanism, while the efferent limb may be synergistically inhibited by these mechanism.[43] These findings may explain why we see such a high predominance of hoarding of urine in patients who have chronic problems with constipation and rectal distention. Distention in the rectal wall generates impulses that are transmitted distally through its walls via the myenteric plexus, activating the rectal sphincteric relaxation reflex and causing smooth muscle relaxation in the internal anal sphincter. The degree of relaxation is in proportion to the fecal volume and the speed at which the rectum is distended. An increase in intra-abdominal pressure lowers the pelvic floor, thereby increasing intrarectal pressure. Relaxation of the external sphincter allows the fecal bolus to be expelled. In many children who have intermittent fecal soiling or fecal marks on the underwear involuntary relaxation of the internal sphincter allows stool to present at the anus, thereby soiling the underwear. When they sense the stool at the anal verge, they clamp down on the external sphincter and the stool is pushed back in. Maintaining this chronic rectal sphincter tone leads to sustained pelvic floor hypertonicity, which may persist during voiding. This may contribute to the detrusor hyperplasia commonly seen in children with constipation.

In agreement with these theories we have noted in our biofeedback patients that we can easily predict whether the child has been compliant with the bowel program. Children who normally do well with biofeedback sessions at times come in unable to relax the sphincter. In these cases the common answer is that they have been off of the bowel program, underscoring the association between the 2 conditions.

There are some theories that the increased fecal mass that is stored in the rectum and sigmoid may exert some type of pressure on the bladder wall. Therefore, this increase in volume in the pelvis decreases functional bladder capacity. The example of a gravid uterus compressing the bladder, leading to urinary urgency in pregnant woman, has been used by some investigators to describe the possible effects of stool in the pelvis leading to bladder instability.[8] It is possible that stretch receptors in the bladder wall can be stimulated by the extrinsic fecal mass, thereby triggering detrusor contractions of various amplitudes and, thus, sustaining a vicious cycle of continued contractions. It is also possible that colonic contractions may be triggering bladder contractions via shared neural pathways in the pelvis or spinal cord as evidenced by findings in patients with imperforate anus.[45] Recently Pezzone[46] and Ustinova[47] et al reported that acute colitis triggers bladder hyperactivity in rats, providing experimental evidence for cross-talk between different pelvic viscera. We noted this in our patients with colitis. When there is an acute flare-up of colitis, there is generally an increase in voiding symptoms. When colitis is controlled, the symptoms cease. Patients can show dyssynergic voiding as well as urgency/frequency in these situations. We have also found that in many young boys presenting with chronic erections and girls complaining of chronic vaginal or perineal pain the conditions have been corrected with a good bowel program. These cross-talk mechanisms support findings in patients with imperforate anus, in those with colitis and even in normal children who have a sudden urge to void associated with gaseous distention or a colonic contraction that at times is imperceptible to them. This cross-talk mechanism underscores the importance of a bowel management program for OAB treatment.

Abbreviations and Acronyms

5-HT	=	serotonin
ATP	=	adenosine triphosphate
NA	=	norepinephrine
OAB	=	overactive bladder syndrome

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EDITORIAL COMMENT

These 2 studies from Dr. Israel Franco force us to rethink the way in which we have traditionally looked at OAB in children, its causes and its management. We must turn from our simplistic way of considering an overactive detrusor as a phenomenon in isolation, but rather define it in more broad terms as a manifestation of several interrelated abnormalities that incorporate bowel function, spinal cord and central nervous system defects together. These potential causes can be inherited in some patients, can appear as a result of subtle changes in fetal development and most importantly can continue to plague an individual as the child matures into adulthood. The emphasis and admonition of this author are something that we as pediatric and adult urologists must share with each other, so as to appropriately treat these children from childhood, when symptoms begin, to adult life, when they can become incapacitating in relation to work and interpersonal relationships. The review of well worn, current and promising treatments gives us the impetus to look at all forms of therapy that might help control the problem as well as develop innovative approaches to this ubiquitous issue, now that we know that its causes stretch beyond just an overactive detrusor muscle. This is a fresh approach to this widely common complaint. The author sounds the clarion call for more research and collegial affiliation between adult and pediatric urologists to find and promote more effective therapies to control this difficult clinical problem.

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