
Overactive Bladder in Children. Part 2: Management

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Purpose: The management of pediatric overactive bladder syndrome has relied primarily on anticholinergics and a bowel regimen. In many cases the results have been ineffective and they have frustrated many parents, patients and practitioners. We explored other treatment modalities that may be more effective than the regimens that we currently use. A thorough understanding of the causes of overactive bladder syndrome are essential to help us find the appropriate treatment for individuals.

Materials and Methods: We looked at numerous treatment modalities that are being used for overactive bladder syndrome and matched them to a specific cause of overactive bladder syndrome that would be best suited to treat the problem. The treatment of constipation as a mainstay for pediatric overactive bladder syndrome was explored as well as its different options. New treatment modalities involving electrical stimulation were explored as well as botulinum A toxin injections.

Results: The effectiveness of each treatment was assessed, thereby providing the reader with a foundation for choosing the appropriate treatment.

Conclusions: The treatment of pediatric overactive bladder syndrome is not as simple as placing children on anticholinergics and, if there is no response, simply saying that they will outgrow it. The causes of overactive bladder syndrome are multifactorial and a better understanding of the pathophysiology will allow us to target treatments appropriately for individuals.

Key Words: bladder; urinary bladder, overactive; physiopathology; constipation

TREATMENT FOR OAB

The mainstay of OAB treatment for years has been anticholinergics but this has begun to change in recent times. Treatment has called for a bowel program, a timed voiding regimen and even biofeedback, which seems to help the majority of children. In those who are refractory it is necessary to consider medications. The first line drug for OAB has been anticholinergics. The result with this group of drugs has been mixed at best. Van Arendonk et al found that in patients who experience wetting on a daily basis the likelihood that anticholinergics would be effective was only 20%, relegating these patients to frustration with the treatment regimen.¹ This study as well as our observations have shown that it is unlikely that patients would respond to anticholinergics if they have frequent wetting and urgency that do not respond readily to a bowel program, timed voiding and biofeedback.

We have found that α -blockers are quite effective for OAB, especially when biofeedback has failed. Many of these patients may show primary bladder neck dysfunction² or external sphincter dyssynergia and α -blockers have been essential for correcting the underlying problem, while using anticholinergics would have simply mollified the symptoms. We reviewed the records of our patients with urgency/frequency syndrome and found that many responded to terazosin for OAB and more responded to this treatment modal-

ity or a combination of terazosin and oxybutynin than to oxybutynin alone (unpublished data). There appears to be a role for α -blockers in OAB beyond bladder neck dysfunction. It appears that α -blocking agents that may have more of a central effect seem to be more effective when there is no evidence of internal or external sphincter dysfunction for decreasing OAB symptoms.

In our series of patients with urgency/frequency syndrome we found that many who were refractory to treatment had increased association with some form of neuropsychiatric problem, ie attention deficit disorder, attention deficit hyperactivity disorder, depression or anxiety, or there was a strong family history of such problems. Many of these children appeared to have resolution of OAB symptoms with appropriate treatment for the underlying neuropsychiatric problems.

The use of tricyclics for OAB is something that has been done in the adult population with some success. We have also used it in our refractory cases and found it to be quite helpful. It appears again that drugs that alter NA homeostasis have a more profound effect in patients with OAB than anticholinergics. The introduction of newer anticholinergics that show high levels in the bladder and possibly bind to muscarinic receptors in the bladder mucosa may have a greater role in OAB management in the future. Unfortunately these drugs are yet to be tested in children for safety and efficacy. A major drawback to OAB medications that work via this mechanism is that frequent urination may not allow for the drug to stay in contact with the mucosa long enough for it to be effective. It is possible that the main reason that other anticholinergics were ineffective is that

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they present limited amounts of the active metabolite to the bladder receptors, thereby limiting their usefulness.

The role of phosphodiesterase inhibitors in OAB is something that needs further exploration. Only time will tell if it may also have a useful role.^{3,4}

TREATMENT FOR CONSTIPATION AND FECAL RETENTION

Correlation of constipation with bladder problems was brought to light in a landmark study in 1997 by Loening-Bauke of 234 constipated children.⁵ Of the patients 29% had daytime urinary incontinence, 34% had nighttime incontinence and 11% had UTIs. After 1 year when constipation was relieved in 52% of the patients, all in whom constipation was completely corrected ceased to have UTIs and 80% had daytime urinary incontinence corrected. Nighttime incontinence was also corrected in 63% of cases. It is interesting to note that children who have had problems with chronic constipation can accommodate a rectal balloon with up to 120 ml before they feel the sensation to defecate. Normal children only accommodate a balloon with a volume of 20 cc before they have a sudden urge to defecate.⁶ This indicates that many of these children have retention of stool in the rectal vaults. Thus, confirmation by parents that the children have bowel movements every day is usually not an adequate reason to assume that these children are not constipated. Constipation can be readily diagnosed in a uniform manner and patient progress can be followed using the Bristol stool form scale, which has been validated in adults and appreciated by children.⁷ A history of chronic abdominal discomfort, particularly periumbilical discomfort, is usually associated with issues of constipation in children who have overactive bladder. It is clear that in many children who are treated for stool problems correction of constipation must be pursued using several techniques.⁸ First and foremost is the introduction and continued use of a high fiber diet and increased fluid intake. The other is some form of stool softener and/or cathartic. This allows the continued propulsion of stool throughout the colon, thereby allowing the colon to shrink with time back to normal levels, when distention sensations can occur at appropriate volumes. The recent introduction of medications such as tegaserod for the management of the irritable bowel syndrome may have a role in the future management of overactive bladder dysfunction.

Tegaserod is a 5-HT₄ agonist that causes increased motility of the gut.⁹⁻¹¹ Studies have indicated that the colon is the largest repository of 5-HT in the body and patients with irritable bowel syndrome with chronic constipation have low 5-HT levels in the gut. Treatment of their constipation with tegaserod may have a dual beneficial effect. Correcting constipation and emptying the colon leads to the elimination of strong peristaltic waves that could prevent strong sudden bladder contractions leading to urge incontinence.

In addition to the mentioned reestablishment of normal 5-HT homeostasis in the colon, possible crossover into the central nervous system may help correct detrusor hyperactivity that may be centrally mediated. We know that Onufrowicz's nucleus is rich in 5-HT receptors and this site also modulates bowel function. Our experience with children who have had refractory overactive bladder with squatting and sudden urge incontinence and who had been on numerous types of bowel programs and were not responding well to all

forms of treatment have responded to treatment for constipation with tegaserod. Control of constipation has led to complete elimination of wetting, detrusor hyperactivity and post-void residual urine. It is unclear whether tegaserod causes a systemic increase in 5-HT or possibly activation of Onufrowicz's nucleus in the spinal cord, thereby altering signaling in the spinal cord or in cortical processing. Animal data indicate that tegaserod has an effect in the spinal cord. It is possible that the better propulsion of the stool and the elimination of unwanted colonic contractions lead to the elimination of detrusor hyperactivity. What we know is that many patients who had been maintained on bowel regimens including GlycoLax™, mineral oil and sennosides, and who were having regular bowel movements but continued to wet or have a large post-void residual urine volume experienced the elimination of OAB symptoms and marked or complete elimination of post-void residual urine when tegaserod was added to the treatment regimen (unpublished data).

BOTULINUM A TOXIN

Botulinum A toxin is the most potent biological toxin known. It was first discovered in 1897 by van Ermegam. It acts by inhibiting acetylcholine at the presynaptic cholinergic junction. Inhibited acetylcholine release results in regionally decreased muscle contractility and muscle atrophy at the injection site. The chemical denervation that ensues is a reversible process since axons resprout in approximately 3 to 6 months. The toxin acts at the neuromuscular junction at the external sphincter to block vesicle transport of acetylcholine, in essence producing chemical denervation. Clinical effects begin within 5 to 7 days and are reversible because terminal resprouting occurs within 6 months. The clinical success of botulinum A toxin is supported by laboratory research showing marked decreases in the release of labeled norepinephrine and acetylcholine in botulinum A toxin injected rat bladders and urethras. While the therapeutic effects of inhibiting acetylcholine release are obvious, blocking norepinephrine release may provide clinical benefit by inhibiting sympathetic transmission in smooth muscle dyssynergia. This is why some patients whom we have treated who had combined internal and external dyssynergia responded well to botulinum A toxin injections.¹²

Botulinum A toxin has also been used to inject the bladder to decrease detrusor hyperactivity. Studies in adult spinal cord injured patients and children with spina bifida have indicated success with multiple injections throughout the floor of the bladder. Botulinum A toxin injections of the detrusor have been performed for nonneurogenic OAB in symptomatic adults with some success. A drawback of this treatment is the need for re-treatment since the probable underlying cause is not in the bladder but elsewhere. Hoebeke et al reported their experience with 15 children, indicating that durable (greater than 12 months) relief of symptoms could be achieved in more than 50% with a single injection.¹³ Only 3 patients did not respond, while those with a partial response appeared to respond to a second injection. These findings are encouraging and could help further the treatment of OAB in children in whom the etiology is not sphincter dyssynergia.

On the other hand, the use of botulinum A toxin injections for sphincter dyssynergia could possibly be beneficial, in that elimination of the dyssynergic voiding pattern could

possibly help eliminate the detrusor hypertrophy that is commonly associated with detrusor overactivity. Botulinum A toxin injection produces reversible chemical sphincterotomy, which avoids a major surgical procedure with its attendant risks. Botulinum A toxin has been used to treat spinal cord injured adults with DSD and children with spina bifida. Its use to treat nonneurogenic DSD was described in 1997 by Steinhardt et al in a neurologically normal child.¹⁴ They injected a total of 20 U in 4 quadrants at the external sphincter in a 7-year-old girl with recurrent UTIs and wetting who had dramatic urethral dilatation due to severe external sphincter dyssynergia. After 18 months the child was infection-free and dry. At the annual meeting of the Section of Urology, American Academy of Pediatrics in 2001 Diaz-Soldano et al presented a series of 20 females with "lazy bladder" and external sphincter spasticity who were treated with botulinum A toxin on a prospective basis.¹⁵ At 2 years of followup the patients had no recurrent UTIs compared with a pre-procedural average of 3 infections per year. However, voiding diaries revealed no statistical differences in voided volumes or voiding intervals. Diaz-Soldano et al favored botulinum A toxin injection with 50 U and concomitant urethral dilation. Their results showed subjective improvements in daytime/nighttime urine flow and they postulated that intravesical pressures after botulinum A toxin were likely decreased. Although the number of UTIs was decreased, Diaz-Soldano et al did not achieve total continence in the patients in their study. Although this study appears to have been flawed for many reasons, it further strengthens the foundation for the use of botulinum A toxin injections in neurologically normal children. More recently a larger series of 20 patients described by Radjovic et al indicated that the treatment of DSD was clearly helped by botulinum A toxin injections in neurologically normal children.¹⁶

We have had exceptionally good results in children in whom we used botulinum A toxin to treat external sphincter dyssynergia of nonneurogenic origin.¹⁷ We injected 12 patients with botulinum A toxin, including 300 U in and around the external sphincter. All 12 patients responded well to the injections with no adverse effects. Only 1 patient had to be re-injected more than once. One girl was on intermittent catheterization and unable to empty the bladder, leaving a post-void residual urine volume of 250 cc at a time. This child is completely dry, has no accidents and voids to completion a year and a half after injection. A boy was offered augmentation cystoplasty to manage intractable wetting and severe DSD, leading to chronic epididymitis. In the limited studies that we have available to date botulinum A toxin represents a viable option for treating DSD. Correcting DSD has led to the resolution of associated OAB symptoms.

BIOFEEDBACK THERAPY

Biofeedback therapy has been used in urology for many years. The use of Kegel exercises was introduced to help patients with stress urinary incontinence. Subsequently in the mid 1990s biofeedback was introduced for treating children who had chronic wetting problems as well as the inability to empty the bladder completely. We started performing biofeedback therapy in 1997 and our program has been extremely successful.¹⁸ Many children in whom initial treatment for constipation failed and who showed signs of external sphincter dyssynergia would undergo biofeedback ther-

apy. Uroflowmetry with concomitant abdominal and perineal EMG would be performed. This study would then indicate external sphincter dyssynergia by increased activity in the perineal sphincter EMG probe. If there was no increased activity in the perineal sphincter probe and there was abdominal straining, internal sphincter dyssynergia would be suggested by the study.

Combs et al reported that with a good EMG/uroflowmetry study internal sphincter dyssynergia can be diagnosed based on an EMG lag time of more than 4 seconds.¹⁹ They found a statistically marked difference in the time required for the urine flow to be recorded from the time that EMG becomes quiescent. This period is called the EMG lag time and it correlates with the more invasive opening time on videourodynamics. These patients would then undergo voiding cystourethrogram or videourodynamics to confirm the presence or absence of internal sphincter dyssynergia. After a diagnosis of external sphincter dyssynergia was made, the patients would then undergo biofeedback therapy. If internal and external sphincter dyssynergia was present, treatment would consist of α -blockers as well as biofeedback. Each session lasted approximately 45 minutes with a trained nurse performing the biofeedback therapy. Initial biofeedback therapy included simple relaxation and contraction exercises while the patient monitored the oscilloscopic activity of the perineum.

The technology has evolved, such that we now use a computerized system with a game-like interactive setting, in which children attempt to move an icon of their choice, ie a dolphin, car or bird, within the predetermined ranges that have been set. This has facilitated the training process and lowered the age at which children can be treated. Preliminary data from our use of this program indicate a decrease in the number of biofeedback sessions required for children to master pelvic floor relaxation.

Biofeedback therapy is limited by the ability of the child to cooperate with the health care provider running the session. Children younger than 5 years are typically incapable of doing biofeedback on a regular basis. Occasionally some children younger than 5 years can be taught to relax the pelvic floor muscles appropriately with biofeedback. Children with significant learning disabilities, behavior problems and other neurological problems are not candidates for biofeedback. Biofeedback therapy is useful for managing overactive bladder, primarily by decreasing outlet resistance during voiding, which leads to detrusor hypertrophy, thereby leading to detrusor instability.

URETHRAL OVERDISTENTION

Management of overactive bladder and bladder instability by urethral dilation is something that has been going on for many years in adult urological practices. Numerous women with urethral syndrome have had the urethra dilated monthly for years. Many of these women have classic symptoms of overactive bladder, pelvic discomfort and dysuria. This urethral syndrome in older women parallels the symptoms that typically would be classified as bulbar urethritis in boys. In boys with bulbar urethritis it was reported that the problem is due to dysfunctional elimination syndrome, most likely because of pelvic floor dysfunction. In these women over dilatation of the urethral sphincter leads to improvement in symptoms. In patients with spina bifida

who have increased outlet resistance management of the external sphincter with over dilation leads to improved bladder capacity.^{20,21} This mechanism of over dilation probably works in a fashion similar to that of botulinum A toxin at the external sphincter level. This temporary sphincterotomy occurs by over distention and/or by tearing the sphincter muscles. Central neural processes may lead to resetting receptors in the spinal cord and possibly in the brain, which may lead to decreased sphincter activity. This decrease in sphincter activity leads to improved bladder emptying due to reduced outlet resistance, thereby allowing the detrusor muscle in the bladder to not work as hard. This decrease in detrusor activity in turn translates to a possible decrease in overactivity at the bladder level.

SPINAL CORD STIMULATION

Spinal cord stimulation is something that has been used with increasing regularity in adult patients. Selective stimulation of the sacral and pudendal nerves has led to significant improvement in overactive bladder in patients who have had stimulators implanted. A recent study by Dasgupta et al indicates that there appears to be significant changes in the ACC when spinal stimulation is activated.²² Their study using positron emission tomography to identify regions of brain activity during bladder filling with and without sacral nerve modulation indicated decreased activity in the ACC and PCC in patients who had problems with urge incontinence. After the stimulators were turned on the activity increased in the ACC and PCC. ACC activity is thought to be enhanced by painful, emotional cognitive and visceral stimulation. The ACC is thought to be part of a network of brain centers involved in the modulation of autonomic responses to noxious stimuli. It is reciprocally connected to other cortical and brain stem centers, including the amygdala, hypothalamus, periaqueductal gray, substantia nigra and ventral tegmental area. Extensive damage to the frontal regions involving the ACC may result in profound motivational impairment or in urge incontinence. More recent functional brain imaging has shown changes in ACC activity with urine storage and micturition. These observations are consistent with a proposal that the ACC supports an integration of visceral afferent information with internal motivational states and external behavior clues to drive facilitatory autonomic and motor responses for adaptive behavior. The activity of the posterior cingulate cortex parallels that of the ACC. PCC activity can interrupt micturition. PCC activity has been characterized as more evaluative. The functional role of the PCC remains elusive. Its role may be to signal that it is proper to empty the bladder before it becomes too full.

These findings with spinal stimulation indicate that the increased activity occurs primarily in the frontal lobes of the brain. Thus, this places voiding control primarily in the cortex. The role of spinal stimulation in children remains to be well defined. There are few if any studies that have been published of spinal stimulation for voiding dysfunction in children.²³

PERIPHERAL NERVE STIMULATION

Electrical tibial nerve stimulation is based on the traditional Chinese practice of using acupuncture points over the common peroneal posterior tibial nerves to inhibit bladder ac-

tivity.²⁴ Transcutaneous posterior tibial nerve stimulation has been evaluated in clinical trials with variable results. The technique involves a 34 gauge stainless steel needle, which is inserted approximately 5 cm cephalad to the medial malleolus just posterior to the margin of the tibia. A stick-on electrode is placed on the medial surface of the calcaneus. More substantial data are necessary but current reports in adults indicate that it is beneficial. Limited reports of its use in children have also indicated efficacy. Hoebeke et al reported that 17 of 28 children who had been refractory to medical treatment had resolution or improvement of symptoms.²⁵ Of 19 patients who had abnormal frequency 16 showed marked improvement. Overall for the group mean bladder capacity increased significantly. This study indicates a role for improvement in overactive bladder in children using peripheral nerve stimulation. The exact mechanism of this modality is unclear. What we can extrapolate from the recent findings with sacral modulation is that electrical tibial nerve stimulation may function in a fashion similar to that of sacral modulation with an effect on the brain.

DISCUSSION

Signs and symptoms of overactive bladder in children can vary dramatically in their typical presentation. Many of these children confess that they have no sense that they are wetting when they have accidents. Other children have a strong urge to void and will be seen clutching the penis or squatting and sitting on their heels in an attempt to prevent incontinence. Other children may manifest overactive bladder simply by having an increased sense to void and voiding quite frequently. Overactive bladder in these cases is thought to lead to increased tonic activity of the external sphincter. This increased tonic activity can lead to chronic tightening and fibrosis of the external sphincter. This chronic tightening and incomplete relaxation of the external sphincter can lead to turbulent urine flow with resultant urethral discomfort, typically called bulbar urethritis. We have reported that bulbar urethritis, which is known as idiopathic urethritis or urethrorrhagia syndrome, is due to pelvic floor dysfunction.²⁶ In these patients the turbulent urine flow disrupts the lining of the urethra and leads to intermittent dysuria and at times bleeding. This syndrome is primarily noted in males but there is an analogous syndrome in females. In some girls we also see dysuria, vaginal pain and gross hematuria. Incomplete relaxation of the sphincter leads the bladder muscle to hypertrophy. This hypertrophy leads to a gradual decrease in functional bladder capacity and increased bladder flow, thereby creating a vicious cycle by which overactive bladder is worsened.

Concomitant increased pelvic floor activity may be associated with increased autonomic stimulation of the perineal organs and musculature. This form of increased autonomic activity has been implicated in interstitial cystitis as well as in erectile dysfunction in males and sexual dysfunction in females. Recent studies indicating an association between erectile dysfunction and lower urinary tract symptoms show that there is some form of heightened sympathetic activity that is common in the 2 situations, leading to pelvic floor dysfunction and erectile dysfunction. Abnormal tilt table testing has been associated with patients who have benign

prostatic hyperplasia, again indicating some form of autonomic dysfunction.²⁷

This association between autonomic dysfunction in patients with overactive bladder has led us to postulate that centrally acting α -blocker therapy may have a greater role in the primary management of overactive bladder. In the last several years the number of patients whom we have treated with α -blockers as a primary treatment modality has increased dramatically. The number of patients being treated with anticholinergic medications for suspected overactive bladder in our hands has decreased. We have also seen a marked increase in our aggressiveness in managing what are suspected to be behavioral or psychological problems. As we aggressively review patient and family histories, we have been finding an ever increasing number of associated psychiatric diagnoses. In many instances when parents are asked bluntly if there is a history of anxiety disorders, depression, obsessive compulsive disorder or another psychiatric issue, we have been finding more and more patients confess that a primary family member has one of these diagnoses. These findings may indicate that the root of voiding dysfunctions may be more centrally than peripherally located. It also may indicate clearly that, similar to the Ochoa syndrome, there is a genetic basis for voiding dysfunctions. A link with anxiety disorders and significant voiding dysfunctions has been reported in the literature.²⁸ A gene site has been found for patients with known anxiety disorders. Managing these suspected behavioral problems with the appropriate medications can lead to marked improvement in overactive bladder problems in patients who were refractory to all methods of treatment. In many instances when a patient is thought to have attention deficit disorder we recommend that they should be seen and evaluated by appropriate personnel. In many instances the child does not improve until treatment for attention deficit disorder or attention deficit hyperactivity disorder has been initiated. In some instances the management of overactive bladder is refractory to anticholinergics and α -blockers. In some of these patients treatment has been facilitated by the introduction of imipramine or 5-HT reuptake inhibitors. Many of these patients seem to respond favorably to the medications, although they do not carry a diagnosis of psychiatric disorders.

The high correlation of abdominal pain, chronic constipation and urinary incontinence, and their subsequent improvement with tegaserod in our experience indicates that there is a clear-cut correlation with voiding dysfunction and serotonergic activity. Further work must be done to look at this. Current clinical trials of duloxetine for stress incontinence and overactive bladder in women have indicated that serotonergic medications may have a greater role in the long-term management of voiding dysfunction.²⁹ More studies must be done of the relationship between voiding dysfunction in children and its role as a predictor of adult mental health. It is safe to say that not all children with overactive bladder have some form of behavioral or psychiatric problem since a large percent respond readily to the correction of constipation. The 20% of children who do not respond to constipation correction are those who may have continued problems as adults with voiding dysfunction. These patients present in adulthood with overactive bladder, stress incontinence, erectile dysfunction, vaginismus, chronic prostatitis, chronic epididymitis and possibly even signs of affective disorders.

CONCLUSIONS

It is becoming apparent that the vesicocentric theories that were proposed in the past for overactive bladder must make way in favor of a more corticocentric way of thinking. Currently anticholinergics seem only able to treat symptoms, while α -blockers appear to treat symptoms but also work at the root of the problem. More research efforts must be made in assessing the central nervous system as the primary site of dysfunction and targeting treatment at these sites. The development or reevaluation of current medications that target central sites is critical to the progression of treatment for OAB beyond the current state. Maintaining the status quo and continuing to believe that treating symptoms is the correct path does our profession and our patients a disservice. Correcting the underlying root cause of the problem should be our goal. It is up to us as physicians to probe deeper into this problem and not accept the status quo, which in many instances may have been built on a foundation that lacked evidence based medicine. Continued advances in functional neural imaging will continue to open up new frontiers in this field and hopefully provide the evidence that is necessary to form the foundation that will serve as the source of answers to our problems. Medications that are developed using the data garnered from this evidence based medicine will hopefully treat the underlying disease process and not just the symptoms. It is increasingly apparent that norepinephrine and 5-HT are critical in the modulation of voiding processes. Treatment with this group of drugs must be explored further. The current stigma associated with the use of 5-HT reuptake inhibitors and the current restrictions imposed by the exorbitant cost of new drugs may inhibit the development of drugs that can affect modulatory effects on voiding neural pathways. The continued use of stimulation modalities, whether peripheral or central, is something that needs continued exploration in the future. The complexity and difficulties that are encountered when doing studies in children must be overcome to allow greater advancement in this field. It is becoming apparent that childhood OAB is a lifelong problem and correcting the problem at a young age may prevent further problems in adulthood. Hopefully device makers and drug manufacturers can recognize this and target treatments for children to prevent what could be more profound adult problems.

Abbreviations and Acronyms

5-HT	=	serotonin
AC	=	cingulate gyrus
ACC	=	anterior cingulate gyrus
DSD	=	detrusor-sphincter dyssynergia
EMG	=	electromyography
OAB	=	overactive bladder syndrome
PCC	=	posterior cingulate gyrus
UTI	=	urinary tract infection

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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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