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The Role of Bladder and Bowel Dysfunction (BBD) in Pediatric Urinary Tract Infections

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Abstract The child with lower urinary tract symptoms, in the absence of neurological abnormalities, represents an increasingly common source of referral to the pediatric urologist. Patients with lower urinary tract dysfunction are at increased risk of urinary tract infections (UTIs), which can be a potential source of expense, inconvenience, and even morbidity and renal impairment. Many of these patients present with concomitant bowel dysfunction in the form of constipation and encopresis. As a result, the term "bladder and bowel dysfunction" (BBD) has been introduced and refers to the close relationship of the bladder and bowel and their interrelated disturbances. An in-depth understanding of BBD and its role in recurrent UTI is the key to treatment and prevention of further morbidity in these patients. We present an updated review of the literature on BBD and UTIs in children, including its pathogenesis, evaluation, and management.

Keywords Bladder and bowel dysfunction · Dysfunctional voiding · Dysfunctional elimination syndrome · Urinary tract infections

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Introduction

Over the past three decades, the association of bowel dysfunction in combination with lower urinary tract symptoms (LUTS) and/or (urinary tract infections) UTIs has become recognized. These diagnostic complexes in children in the absence of neurogenic abnormalities represent an increasingly common problem for primary care providers and in subspecialty care including, gastroenterology, pediatric surgery, mental health practices, and pediatric urology. These children often present with UTIs or, because of symptoms resembling UTI, are mislabelled and hence inappropriately investigated and treated. Such issues can lead to frustration of the families and children themselves. There is the potential for significant morbidity in the most extreme cases. Although the majority of patients respond well to therapy, practitioners have had to broaden their perspective, in order to assure that attention is paid to both the bladder and the bowel in these patients. We present a review and provide a practical approach for those clinicians caring for neurologically intact children with BBD in the setting of urinary tract infections.

Terminology

Various terms have been used to characterize symptom complexes and the severity of related pathologies in patients with urinary complaints, including Hinman syndrome [1], underactive bladder, dysfunctional voiding, and more recently, dysfunctional elimination syndrome (DES) [2] and bladder and bowel dysfunction (BBD) [3••]. They represent a spectrum rather than a single entity, but all attempt to describe and classify voiding abnormalities that are nonneurogenic in origin (Table 1). In 2006, the Standardization Committee of the International Children's Continence Society defined "dysfunctional voiding" as an entity occurring in a "neurologically

Table 1 ICCS terminology for BBD and related conditions [3••]

Conditions	ICCS definition
Hinman syndrome	"…When severe BBD results in changes in the upper urinary tract (e.g. hydronephrosis and/or vesicoureteral reflux, it may be synonymous with the historical term 'Hinman syndrome'." [3••]
Underactive bladder	"…children who need to raise intra-abdominal pressure to initiate, maintain or complete voiding i.e. straining."
Dysfunctional voiding	"…habitually contracts the urethral sphincter or pelvic floor during voiding and demonstrates a staccato pattern with or without an interrupted flow on repeat uroflow when EMG activity is concomitantly recorded…associated with a neurologically intact patient." [3••]
Dysfunctional elimination syndrome (DES)	"We discourage using the term…as this connotes a particular abnormality or condition." [3••] Koff et al. was the first to describe DES as "functional bladder and bowel disturbances…which include bladder instability, infrequent voiding, the Hinman syndrome and constipation." [2]
Bladder and bowel dysfunction (BBD)	"[A] descriptive comprehensive term of a combined bladder and bowel disturbance that does not explain pathogenesis but rather encompasses this parallel dysfunction." [3••]
Severe BBD	"…characterized by LUT and bowel dysfunction seen in children with neurologic conditions who have no identifiable or recognizable neurologic abnormality." [3••]

intact child" with "habitual contraction of the urethral sphincter during voiding, as observed by uroflow measurements" [4]. This term is limited to children who have had investigation with uroflowmetry and electromyography (EMG). In addition, this term fails to recognize the role that bowel dysfunction (e.g., constipation, encopresis, functional fecal incontinence, etc.) plays in patients presenting with lower urinary tract dysfunction. In the 2014 updated report from the International Children's Continence Society (ICCS), the term "bladder and bowel dysfunction (BBD)" was used to emphasize the important relationship of the bowel in lower urinary tract dysfunction [3••]. This is preferred over "dysfunctional elimination syndrome," which implies that a specific abnormality exists. For the purposes of our review, we also prefer the term bladder and bowel dysfunction as an inclusive term that recognizes this relationship between the bladder and bowel.

Pathophysiology of BBD

Bladder filling and emptying is under the control of central and peripheral neural pathways. Parasympathetic nerve fibers arise from sacral nerve roots (S2 to S4) and run in the pelvic nerve, to control bladder contraction during voiding and relaxation of the smooth muscle sphincter during micturition. Sympathetic nerve fibers arise from thoracolumbar nerve roots (T10 to L2) and run in the hypogastric nerve and sympathetic chains, to stimulate bladder storage and contraction of the smooth muscle sphincter during the storage phase. The pudendal nerve that arises from S2 to S4 is integral to volitional control of the external sphincter. Central control of these mechanisms occurs in the sacral micturition center, pontine micturition center (PMC), cerebellum, basal ganglia, limbic system, thalamus, hypothalamus, and cerebral cortex. Voiding requires coordination of the bladder-sphincter complex, with simultaneous bladder contraction and relaxation of the bladder outlet [5].

There is a clear progression in voiding pattern throughout life—from the uncoordinated, frequent voiding pattern in infancy to a mature adult voiding pattern that fills and empties during socially appropriate times. Voiding occurs as frequent as 10 to 15 times per day toward the end of the first year of life, decreasing to 8 to 10 times per day in the following 2 to 3 years and eventually reaches 4 to 6 times per day by age 12. This also corresponds to an increase in bladder capacity over time, which occurs disproportionately greater than the increase in urine output. As early as the neonatal period, it is thought that there is already central and peripheral control of micturition, rather than simple spinal reflexes alone. Infants are thought to have elevated detrusor pressures during voiding and have an interrupted or "staccato" pattern, suggestive of detrusor-sphincter incoordination. As the child reaches the second or third year of life, they enter the "toilet training" phase and begin to develop voiding patterns more similar to adults. This is due to a variety of factors, including an increase in bladder capacity, awareness of bladder filling and the urge to urinate, improved control over the bladder-sphincter complex, social norms with regard to urination, and the ability to withhold voiding until socially appropriate times [6].

In recent years, there has been increasing support for the relationship between bladder and bowel dysfunction. It has been reported that 58 % of children presenting with lower urinary tract symptoms to a tertiary pediatric urology outpatient clinic also met the criteria for functional defecation disorders by Rome III criteria (see Table 2) [7]. Koff et al. described the term dysfunctional elimination syndrome (DES) when examining the role of DES in children with vesicoureteral reflux (VUR). He identified that VUR resolution was significantly delayed in the setting of DES [2]. This finding supported the use of timed voiding, stool softeners, laxatives, and dietary modifications for constipation for

Table 2 Rome III pediatric criteria for functional GI disorders (adapted from Rasquin et al. [64])

Functional constipation
Must include two or more of the following in a child with a development age of 4 years or older with insufficient criteria for a diagnosis of irritable bowel syndrome (criteria fulfilled for at least 2 months before diagnosis):
2 or fewer defecations per week
1 or more episodes of fecal incontinence per week
History of retentive posturing or excessive volitional stool retention
History of painful or hard bowel movements
Presence of a large fecal mass in the rectum
History of large diameter stools that obstruct the toilet
FNRFI (nonretentive fecal incontinence)
Must include all of the following in a child with a developmental age of at least 4 years (criteria fulfilled for at least 2 months before diagnosis):
Defecation in places inappropriate to the social context at least once per month
No evidence of an inflammatory, anatomical, metabolic, or neoplastic process
No evidence of fecal retention

patients with DES, particularly in the setting VUR. Another study found that children with chronic constipation and urinary incontinence or recurrent UTIs had resolution of their urinary symptoms when the constipation was successfully treated [8].

Several theories support the concept that bladder function/dysfunction is closely tied to the bowel. Both the bladder and bowel share a common embryological origin and neurological pathways [9]. In the fifth to sixth week of embryological development, the urorectal septum descends to separate the cloaca into the urogenital sinus and rectum [5]. Distention of the rectum that occurs in the patient with constipation can cause external compression onto the nearby trigone and bladder neck, leading to detrusor overactivity and bladder outlet obstruction, respectively [9, 10]. Moreover, 43 % of children with encopresis have contraction of the anal sphincter during defecation [11]. Failure of the pelvic floor to relax during micturition and defecation can lead to dysfunction in both respects. Therefore, the term dysfunctional voiding more aptly has been replaced with the terms dysfunctional elimination syndrome or more recently, bladder and bowel dysfunction (BBD), which recognizes the often overlooked role of bowel dysfunction in children with nonneurogenic voiding symptoms. Optimizing both bowel and bladder function is key to evaluation and management of these children.

The Relationship Between Bladder and Bowel Dysfunction and Urinary Tract Infections

Lower urinary tract dysfunction has been thought to be linked to UTIs for a number of reasons. Contraction of the urethral sphincter during micturition can lead to incomplete emptying of the bladder and urinary stasis, which can allow microorganisms to propagate in the urine [12]. Hellstrom et al. examined data from school-aged children in Sweden and compared their questionnaire results regarding micturition habits and urinary incontinence to their prior UTI history. In this study, it was found that there was a relationship between urinary symptoms and a history of UTIs, but the temporal relationship was not studied, and therefore, a causal relationship could not be made [13]. A retrospective review of 257 boys and 366 girls presenting with lower urinary tract symptoms found that 33 % had a history of UTIs [14]. A multivariate analysis by Chen et al. found that UTIs were not associated with dysfunctional elimination syndrome alone. However, in the setting of DES and VUR, the odds ratio nearly doubled [15]. In terms of UTI as a potential cause of lower urinary tract dysfunction, a prospective treatment trial found no correlation between scores on a standardized dysfunctional elimination syndrome questionnaire and a prior history of UTI diagnosed before age 2 [16]. In patient with encopresis, fecal soiling can also introduce gastrointestinal organisms to the periurethral environment. There is data to support the treatment of constipation and encopresis to reduce the risk of UTI [8].

The Relationship Between Bladder and Bowel Dysfunction and Vesicoureteral Reflux

As previously mentioned, the term dysfunctional elimination syndrome was first used in patients with primary vesicoureteral reflux by Koff et al. [2]. In this series, DES was associated with delayed reflux resolution and increased rate of breakthrough UTIs. Correction of BBD may be more beneficial for preventing UTIs in patients with VUR than those without a history of VUR [15]. The 2010 American Urological Association (AUA) Guidelines Committee on Management of Primary Vesicoureteral Reflux in Children performed a comprehensive review of the literature on BBD and VUR. They found that BBD was associated with a lower rate of spontaneous VUR resolution, breakthrough UTIs, lower rate of correction with endoscopic surgery, and increased ureteral reimplantation surgery in patients with VUR [2]. In addition, they recommended treatment for constipation in children with BBD and VUR and feel that prophylactic antibiotics are warranted in this group, especially if there is evidence of renal cortical damage [17].

Evaluation

In children who present with BBD and/or UTI, the evaluation starts with a focused history and physical examination. The urological history should elicit storage and voiding symptoms, associated symptoms, and clues that point toward BBD, such as holding maneuvers (e.g., Vincent's curtsey), urinary incontinence, signs of urgency, and associated behavioral disturbances [18–20]. With regard to bowel function, it is important to ask about stool firmness, frequency, pain with defecation, and encopresis [21••]. Many will not corroborate a bowel history, especially if the child is not encopretic, but upon further questioning, may admit to chronic abdominal pains. With regard to UTIs, it is crucial to confirm that the diagnosis was confirmed by a properly obtained urinalysis and whether it was associated with other symptoms, in particular, fever. Such documentation will avoid the common mislabelling that occurs when symptoms mimicking UTI are falsely attributed as being a UTI. Physical examination should include an abdominal and genital examination. In addition, a focused neurological examination and examination of the sacrum and lower extremities are crucial to rule out an occult neural tube defect as a cause of urinary and bowel symptoms. The ICCS recommends a digital rectal examination in children who fulfil 1 of 6 Rome III criteria (Table 2) to aid in the diagnosis of constipation [21••].

Useful tools on further visits to supplement the initial history include a bladder diary and information on bowel movements. Bladder diaries vary in comprehensiveness, from a 48-h frequency and volume chart to a 7-day bladder diary, encompassing symptoms of urgency and incontinence episodes. Paper-based bladder diaries can be mailed to patients and families before their scheduled consultation, or alternatively, mobile apps may be more practical for older children and adolescents. The Dysfunctional Voiding Symptom Score (DVSS) is a validated questionnaire developed to evaluate 10 voiding dysfunction parameters, for a total score of 0 to 30 [22, 23]. For patients with a component of constipation and/or encopresis, a 7-day stool chart referencing the Bristol Stool Form Scale [24] may be useful for parents and clinicians. The Rome III criteria (Table 2) is recommended by the ICCS for diagnosis of functional defecation disorders in children and is widely accepted in both clinical and research settings [21••].

In recalcitrant cases and in some instances as a baseline, "noninvasive urodynamics," electromyography (EMG), uroflowmetry, and postvoid residual (PVR) measurement may be added. Formal urodynamics are usually reserved for patients at the severe end of the spectrum and those who do not respond to therapy. However, an estimated 10 % of children who present with lower urinary tract symptoms are evaluated with such formal urodynamic studies. In one cohort of patients presenting with nonneurogenic voiding disorders, 10 % of patients were actually evaluated with videourodynamics [25].

Imaging has a role in select cases, but again is not a routine. In children where the history of constipation is not validated or as commonly occurs, not believed to be an issue by the "doubting" family, a KUB and/or ultrasound is often a useful adjunct. One study found that a rectal diameter >30 mm on pelvic ultrasound was associated with rectal impaction, and its authors have advocated for its use over digital rectal examination [26]. Select cases may warrant further investigation with nuclear renography and/or voiding cystourethrogram (VCUG), especially if there has been recurrent febrile UTIs and/or an ultrasound suggesting renal involvement. In addition, magnetic resonance imaging of the spine may be indicated in select cases where a neurogenic cause is suspected. In children who present with refractory LUTS and a sacral skin lesion (e.g. sacral dimple, macula, focal hypertrichosis, nevus, or lipoma), 37 % were found to have a sacral abnormality on MRI. In this study, sacral skins lesions were predictive of occult spinal dysraphisms, while urodynamic findings were not [27]. In patients with occult spinal dysraphism and skin lesions, abnormal urodynamic studies were predictive for the requirement of neurosurgical intervention [28].

Management

After identifying children with BBD, it is important to have a systematic approach to improving voiding and defecation. Therapy should be individualized and tailored to each patient. Clear explanations to the family are mandatory. Without the cooperation of the child him/herself, interventions can be frustrating to parents and providers. A summary of management options for BBD is outlined in Table 3.

Conservative Management

First-line therapy for BBD includes behavioral strategies to improve micturition and defecation. The ICCS uses the term "urotherapy" to describe the "conservative-based therapy and treatment of LUT dysfunction and encompasses a very wide field of healthcare professionals." This includes information and demystification, instruction, lifestyle advice registration of symptoms and voiding habits, and finally, support and encouragement to the patients and caregivers [3••].

First, a review of the bladder diary in clinic often reveals inadequate fluid intake. Increasing fluid intake offers the benefit of increasing urine flow and, therefore, decreasing urinary stasis that may potentially lead to UTIs. Furthermore, timed voiding decreases the interval of time between voiding and, potentially, the time in which bacteria can multiply in the urinary system. This also aims to reduce the volume of urine in the bladder and potentially reduces the risk of urinary incontinence associated with a full bladder. If behavioral abnormalities are present, appropriate psychiatric or psychological referral for diagnosis and management is warranted [20]. Other therapies that have gained popularity in the adult population for reducing UTIs include cranberry juice [29] and probiotics [30]. Even in the adult literature, the data is controversial, and while there is an added cost and significant

Table 3 Summary of management options and indications for BBD (see text for details)

General	Specific	Indications
Urotherapy	Information and demystification Instruction	All patients [3••]
	Lifestyle advice registration of symptoms and voiding habits	
	Support and encouragement to the patients and caregivers [3••]	
Constipation management	Education about bowel physiology and functional bowel disorders Disimpaction	Constipation and/or encopresis [21••]
	Prevention of reaccumulation of feces	
	Behavioral therapy [31]	
Biofeedback		Evaluation suggestive of emptying failure and/or elevated PVR [34, 35•]
Pharmacotherapy	Antibiotics	Recurrent UTIs
		VUR (select cases) [17]
	Alpha-blockers (e.g., doxazosin, tamsulosin)	Evaluation suggestive of emptying failure and/or elevated PVR [36–40]
	Anticholinergics	All patients refractory to urotherapy [42–50] (Caution in patients with urinary retention or severe constipation)
	Botulinum toxin A injections	All patients refractory to urotherapy and/or oral therapies [52–55]
Clean intermittent catheterization		Elevated PVR [56]
Surgery	Endoscopic reflux surgery Ureteral reimplantation	VUR (select cases) [17]
	Augmentation cystoplasty Appendicovesicostomy (Mitrofanoff)	Severe BBD refractory to urotherapy, biofeedback, and/or pharmacotherapy [57, 58]
	Appendicostomy (ACE) Cecostomy tube	Severe constipation and/or encopresis refractory to constipation management [21••, 59 60, 64]
	Colon resection	Severe constipation and/or encopresis refractory of ACE or cecostomy tube [21••, 61, 64]

variability in the products available to the consumer, the harm is likely minimal. Finally, education about normal urinary tract function and dysfunction, as well as support for patients and caregivers, is key.

Constipation and Encopresis

An aggressive bowel regimen is important for constipation and encopresis, in the setting of BBD and UTIs. Mugie et al. described a four-step approach to childhood constipation, including education about bowel physiology and functional bowel disorders, disimpaction, prevention of reaccumulation of feces, and behavioral therapy [31]. Disimpaction is a key first step before maintenance therapy can be initiated. In a prospective, randomized controlled trial, oral polyethylene glycol (PEG) 3350 (1.5 mg/kg/day for 6 days) and rectal enemas have been shown to be equally effective in children with rectal fecal impaction and should both be considered for first-line therapy. However, children who received rectal enemas had fewer fecal incontinence episodes and watery stools but more abdominal pain [32]. Maintenance therapy may be required for a period of months to years. In a Cochrane review, PEG was found to be superior to lactulose with regard to stool frequency, stool form, relief of abdominal pain, and need for additional products [33]. The role of dietary fiber and probiotics remains unclear and inconclusive [21••]. Pediatric gastroenterologist referrals may be made in cases of refractory functional constipation after 6 months of therapy [21••].

Biofeedback

Urinary tract infections associated with BBD may arise from urinary stasis and an inability to empty the bladder due to incoordination of the pelvic floor. The goal of biofeedback is to improve relaxation of the pelvic floor and facilitate emptying during micturition and defecation. It uses electronic or mechanical feedback to guide the patient to the desired endpoint, such as a desired EMG tracing, optimal uroflow curve, or a parameter incorporated into a game. A recent meta-analysis of 27 studies found the level of evidence for biofeedback in BBD to be “fair,” which includes only one RCT. This RCT compared biofeedback to pelvic floor exercises and did not show a statistically significant difference between the two groups [34]. Overall, based on this meta-analysis, there was an 83 % improvement in recurrent UTIs in patients with BBD who underwent biofeedback [35•].

Pharmacologic Therapy

Breaking the cycle of UTI and ongoing elimination issues poses a challenge. While the bowel and bladder are being addressed, a primary goal is to minimize the occurrence of UTI if possible. Antibiotics have been the mainstay of therapy and prophylaxis for urinary tract infections. As noted earlier, current AUA guidelines recommend them in the presence of coincidental BBD and VUR, especially if there are coincidental renal cortical changes [17]. They acknowledge the controversies in the use of routine prophylactic antibiotics in all patients with VUR but strongly support their use in this unique subpopulation of patients.

Alpha-blockers are increasingly used in patients with neurogenic bladder and gaining interest in BBD, particularly with primary bladder neck dysfunction [36]. Their use is limited by a lack of safety data and use is currently off-label, which patients and families must be advised of. In 1999, Austin et al. reported the use of doxazosin (0.5–1 mg nightly, titrated to response as tolerated) in 17 children with both neurogenic and nonneurogenic causes of poor bladder emptying. This initial series reported improvement in symptoms and/or postvoid residual volume in 82 % of patients and was well-tolerated in all but one patient, who developed hypotension [37]. Several studies have shown safety and objective improvement in PVR in patients who had dysfunctional voiding or "primary bladder neck dysfunction" [38–40]. In a double-blind placebo-controlled trial of doxazosin (0.5 mg daily) versus placebo, there were no significant differences in incontinent days per week, severity of incontinent episodes, or alterations in uroflowmetry patterns. However, there was a trend toward a benefit in number of incontinent episodes per week in the doxazosin group. Interestingly, there was a benefit in dysfunctional voiding scores and parental perception in the doxazosin group over placebo [40]. However, the use of doxazosin in this population should not be entirely dismissed. Critiques of this trial include the fixed low dose of doxazosin, small sample size, and a lack of sample size calculation [36]. Larger, randomized placebo-controlled trials are needed to establish their role in BBD and, in particular, recurrent UTIs.

In a nonrandomized study, patients with dysfunctional voiding and elevated PVR underwent biofeedback versus doxazosin (0.5 to 2 mg). Both groups were shown to have an improvement in PVR and urge incontinence episodes. Parental satisfaction was higher in alpha-blocker group, in therapy-responsive children [41]. This suggests that alpha-blockers may be an alternative to biofeedback.

Anticholinergic medications, such as oxybutynin and tolterodine, have been shown to be safe and effective in children with overactive bladder and urinary incontinence [42–45]. Oxybutynin is available in both oral and transdermal formations, while tolterodine is only available in an oral tablet. In recent years, there has been increasing interest in tolterodine in children due to tolerability profile [46]. In patients who crossed over from oxybutynin to tolterodine due to side effects, 77 % of these patients were able to continue on tolterodine with no significant side effects [47]. Munding et al. reported a retrospective series of 30 pediatric patients diagnosed with dysfunctional voiding treated with tolterodine (ranging from 1 mg BID to 4 mg BID) and behavioral modification. They found that a third of patients had a resolution in wetting episodes, while 40 % had improvement and 27 % showed no improvement. Although five patients in this series had a history of urinary tract infections, they did not report whether tolterodine had an effect for these patients [48]. Two other studies examining tolterodine with behavioral modification found an improvement in mean DVSS scores [45, 49]. Dosages for these studies are highly variable, with short-acting tolterodine ranging from 1 to 4 mg BID and long-acting tolterodine ranging from 2 to 4 mg OD. Ayan et al. reported randomized study of 72 patients, comparing tolterodine (1 mg BID) with behavioral modification versus behavioral modification alone versus placebo with behavioral modification. In all three groups, there was a significant decrease in DVSS scores at 1 month. In addition, the tolterodine group had significantly lower mean DVSS scores than the groups who received behavioral modification alone or with placebo, at 1 and 3 months [50]. While there is evidence of symptomatic improvement in children with BBD on anticholinergics, their effect on UTIs is unclear. For patients with BBD on anticholinergics, monitoring, prevention, and treatment of constipation is of upmost importance.

Injection of botulinum toxin A has been used for a number of urologic disorders, including intrasphincteric injections for detrusor sphincter dyssynergia (DSD). A recent meta-analysis concluded that there was insufficient evidence to support its use for DSD in pediatric patients [51]. Nevertheless, there may be a role for patients with BBD who are refractory to or unable to tolerate other conservative and pharmacologic therapies. Steinhardt et al. described its successful use in a "dysfunctional voider," who presented with daytime wetting and recurrent UTIs. After periurethral injection of botulinum toxin A, she was infection-free and off antibiotics at 18-month follow-up [52]. Radojicic et al. reported a small series of 20 patients with recurrent UTIs, "voiding dysfunction," and a high postvoid residual volume refractory to biofeedback and alpha-blockers, who received botulinum toxin A injected transperineally into the pelvic floor and/or external sphincter. All patients were infection-free at 9- to 14-month follow-up, with only one patient on antibiotic prophylaxis [53]. In a series of eight patients, Vricella et al. reported an improvement in voiding parameters (e.g., PVR, flow rate) in 67 % of patients, and half of the patients required a second injection at 15 months [54]. For pelvic floor and/or external sphincteric injections, the pediatric literature supports the use of 50 to 100 units of botulinum toxin A [55].

Clean Intermittent Catheterizations

In children with a large PVR, urinary stasis is postulated to be the cause of UTIs. The literature for clean intermittent catheterizations in children with BBD is limited. Pohl et al. presented a series of 23 patients with dysfunctional voiding and elevated PVR, who were managed with clean intermittent catheterizations. None were reported to have received behavioral modification or biofeedback. At baseline, 9 % had documented VUR, 39 % had concomitant constipation, and 52 % had voiding pressures >40 mmHg. PVR volumes range from 30 to 517 cc (20–113 % of maximum bladder capacity) on urodynamics. With regard to UTIs, 70 % of patients had a history of UTIs, and after initiation of CICs, there was reportedly a five-fold reduction in symptomatic UTIs. No febrile UTIs occurred [56]. Silay et al. retrospectively reviewed 22 patients with Hinman syndrome; all patients had a history of at least one urinary tract infection. Patients were followed for a median of 80.9 months, and all were on CICs at one point. During follow-up, 22.7 % had at least one febrile urinary tract infection [57]. The benefits of reducing urinary stasis must be outweighed by the risk of bacteriuria, cost, urethral stricture, and discomfort, particularly in neurologically intact patients with a sensate urethra.

Surgical Therapy

The role of surgical therapy in patients with BBD and UTIs is limited, as the majority are managed conservatively, at least initially. However, surgery may become indicated in the setting of VUR, BBD, and recurrent breakthrough UTIs, especially if the kidneys appear to be at increased risk. Either open or endoscopic intervention is recommended by the recent AUA guidelines in such scenarios. Success rates after endoscopic management is lower in the setting of BBD compared to no BBD, whereas there is no difference after ureteral reimplantation surgery, according to a systematic review. The presence of BBD also increases the risk of postoperative UTI. These guidelines support the treatment of BBD prior to surgical therapy, although a standard treatment plan for BBD cannot be recommended [17].

In severe cases of BBD associated with UTIs (e.g., Hinman syndrome), surgery may be considered in rare cases of refractory recurrent UTIs and/or risk to the upper urinary tracts. In patients who are at risk of upper tract deterioration due to severe BBD, augmentation cystoplasty with or without appendicovesicostomy (Mitrofanoff) is an option when other measures fail. As mentioned previously, Silay et al. presented a series of 22 patients with Hinman syndrome, and 8 patients (36 %) ultimately required augmentation cystoplasty with Mitrofanoff creation for recurrent UTIs, the presence or worsening of hydronephrosis, or decreased bladder capacity. At follow-up, all had preservation of renal function and none developed chronic renal disease. Postoperative UTIs were not mentioned in the paper [57]. Handel et al. reported a series of four patients with Down's syndrome (trisomy 21) with febrile UTIs and/or urosepsis in the setting of severe dysfunctional elimination syndrome. The two patients who went on to bladder augmentation and appendiceal Mitrofanoff creation were independently catheterizing through the stoma at a follow-up of greater than 5 years [58].

Similarly, severe cases of functional constipation may require surgical intervention. The antegrade continence enema (ACE) was first described by Malone et al. and uses an appendicostomy to instill solutions that can be used to evacuate the colon and rectum [59]. Success rates for the use of ACE in functional constipation ranges from 52 to 92 %. A cecostomy tube serves the same function and can be placed percutaneously [60]. Colon resection is associated with a high failure rate and should only be considered if refractory to ACE or cecostomy tubes [21••, 61].

The goal of therapy is to reduce the risk of UTI and other sequelae of BBD, while minimizing the morbidity of therapy. In a patient who presents with UTIs in the setting of BBD, it is important to approach treatment in a step-wise approach, starting with the least invasive options first. When it comes to BBD therapies that reduce the risk of UTIs, the data is lacking and often not reported in studies. Many studies are also retrospective and lack control subjects. Comparison of different studies is further complicated by lack of consistent terminology. In a study examining urotherapy in patients with dysfunctional voiding, 40–68 % of patients on urotherapy were infection-free during the 12-month period of the study [62]. In a study of 234 children with constipation and/or encopresis, 11 % had a history of UTI. In the follow-up period of greater than 12 months, 52 % of patients were successfully treated for constipation and/or encopresis, and all of the successfully treated patients with UTIs in the absence of renal anatomic abnormalities were infection-free [8]. Biofeedback has been shown to have a 83 % improvement rate in UTIs in patients with dysfunctional elimination syndrome, according to a systematic review of 26 case series [35•]. There is no strong evidence to support the use of alpha-blockers [63] or anticholinergics to prevent UTI, although they have other beneficial effects in BBD [36–40, 42–50]. In the literature regarding open surgery for Hinman syndrome (i.e., augmentation cystoplasty and Mitrofanoff) [57, 58] and severe functional constipation (i.e., ACE, cecostomy tube, colon resection) [21••, 59–61], UTI rates both before and after surgery are often not reported. UTIs in the setting of BBD represent an understudied area of pediatric urology, and more prospective studies are needed to guide evidence-based practice.

Conclusions

There is increasing literature to support the relationship between bladder and bowel function. BBD has been shown to predispose children to UTIs, while modification of bowel and bladder habits has been shown to reduce UTI risk. As a result, all children who present with UTIs should be evaluated for BBD. Those who are diagnosed with BBD should be given adequate education, support, and counselling with an initial focus on conservative therapies. In refractory cases, further investigation with selective noninvasive urodynamics and imaging can help guide management. An individualized plan is essential in determining which case requires the addition of pharmacotherapy, with surgical intervention being a final last resort.

Compliance with Ethics Guidelines

Conflict of Interest Linda Lee declares no conflict of interest. Martin Koyle reports that he has previously received payment, outside of the submitted work, for his work developing educational presentations on behalf of Salix Pharmaceuticals.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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