Chapter 8
Common Bladder Management Treatments for Patients with Neurogenic Bladder

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Introduction

The neurologic control of bladder function is very complex; however, when reduced to simple terms, neurogenic lower urinary tract dysfunction (NLUTD) causes problems with two aspects of bladder function, *Storage* and *Voiding*. The *Storage* phase of bladder function is dependent upon active relaxation of the bladder wall leading to very low-pressure storage even as volume increases. The ability to store is often impacted by neurogenic bladder (NGB) and commonly results in incontinence from bladder spasticity. In addition, loss of normal innervation of the bladder can cause progressive fibrosis in the bladder wall and worsened compliance. This stiffening of the bladder wall leads to bladder contraction and a failure to store adequate volumes within the bladder. Poor bladder compliance, in some cases, can cause very high pressures within the bladder leading to reflux of urine, hydronephrosis, and renal insufficiency or renal failure. High bladder pressures are also highly associated with urinary tract infection, urosepsis, and urinary calculi [1].

The *Voiding* phase of bladder function is also often impacted by NGB. Commonly, voiding dysfunction manifests itself as impaired or absent bladder emptying. This impairment might be a minor annoyance to patients who have to strain or wait for some time for their bladder to empty or it can be much more of a problem and patients may not be able to empty at all. This is very common in disorders such as multiple sclerosis (MS), spinal cord injury (SCI), and Parkinson's. When patients cannot empty effectively they most often have to rely on some type of assisted emptying. Assisted emptying of the bladder can involve physical maneuvers such as Valsalva or Crede voiding, use of catheters, or surgery.

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Medical Management

Current medical management of NLUTD is concentrated upon control of *Storage* symptoms [1]. Multiple classes of medicines act to decrease bladder spasticity, as well as improve compliance in the bladder wall. Anticholinergic drugs, also referred to as antimuscarinics, are a mainstay of therapy for the management of *Storage* symptoms. Some other drugs can complement the effects of antimuscarinics upon the bladder dynamics, and a new class of drug (β3-adrenergic agonist) has gathered some evidence of efficacy for NLUTD storage symptoms.

The only drug currently used for *Voiding* dysfunction, at least within the United States, is bethanechol, which is a muscarinic agonist and has been used historically to augment bladder contraction. Unfortunately, the drug is not very efficacious and is associated with abdominal distention and pain [2]. Bethanechol is not commonly employed in neurogenic bladder management by most clinicians today.

Anticholinergic Drugs

Anticholinergic drugs act to decrease bladder overactivity and improve compliance in the bladder wall. The exact action of these drugs is not perfectly understood, but a simplistic explanation is that the drugs block the muscarinic receptors in the detrusor muscle and their ability to contract when acetylcholine is released at the motor endplate [3]. This mechanism has been suggested to be more complex and may involve inhibition of acetylcholine release from the afferent nerves through feedback from muscarinic receptors blocked in the urothelium or elsewhere in the bladder.

There are many anticholinergic drugs available (Table 8.1). Common side effects of anticholinergic drugs include dry mouth, constipation, and loss of mental acuity. These effects are related to metabolites created by first pass metabolism in the liver. Transdermal administration or extended release medications minimize these therapy limiting side effects. The majority of studies have investigated anticholinergics in patients with overactive bladder rather than NLUTD from NGB.

Recent literature has evaluated the use of two different anticholinergic medicines (oxybutynin and trospium) at the same time [4]. Investigators found that urinary incontinence episodes and bladder capacity had dramatic improvement with monotherapy with trospium and that combined therapy had no additional benefit. They also found that full continence was not common and that even incontinent patients' urodynamics commonly showed persistence of bladder spasticity with high pressures causing detrusor overactivity incontinence.

Another recent study, called the SONIC trial, reported the effects of solifenacin, as well as oxybutynin on urodynamic parameters and patient-reported outcomes [5]. Both solifenacin 10 mg and oxybutynin 15 mg substantially improved maximum cystometric capacity, as well as multiple other measures of bladder function compared to the placebo arms. The effects of the drugs appeared to be almost identical on primary and secondary outcomes. Oxybutinin had worse dry mouth associ-

Table 8.1 Drugs used for medical management of neurogenic bladder lower urinary tract dysfunction.

Drug class/mechanism	Drugs	Dosing	Comments
Anticholinergics: Block acetylcholine receptors at the detrusor muscle motor endplate	Fesoteridine	ER 4,8 mg	Extensive evidence in treatment of NLUTD, ER formulations minimize common side effects, such as dry mouth, constipation, blurry vision, and loss of mental acuity
	Oxybutynin	IR 5 mg, ER 5,10,15 mg, TD gel 100 mg, patch 3.9 mg	
	Solifenacin	5, 10 mg	
	Tolteridine	IR 1,2 mg, ER 2,4 mg	
	Trospium	IR 20 mg, ER 60 mg	
β3-adrenergic receptor agonist: Relaxation of bladder during filling phase	Mirabegron	ER 25,50 mg	Limited evidence for use in combination with anticholinergics or as monotherapy
Alpha adrenergic blocker: Multiple effects in the bladder, acts additively with combination of anticholinergics	Tamsulosin	0.4 mg	Limited evidence in combination with anticholinergic medicines
Tricyclic antidepressants: Anticholinergic like effects	Amitriptyline	10, 25 mg	Limited evidence in combination with anticholinergic medicines

IR immediate release, *ER* extended release, *TD* transdermal, *NLUTD* neurogenic lower urinary tract dysfunction.

ated with therapy; however, the study did not use sustained release medications, which has been shown to decrease this effect.

Transdermal delivery of oxybutynin has been studied in SCI patients with NLUTD [6]. This study was an open label titration study with endpoints including number of daily catheterizations and urodynamic parameters. All of the endpoints were positively impacted by use of the drug and patients tolerated up to three times the normal dose of the drug with only 8% experiencing dry mouth. Additionally, adverse events were not dose related; albeit the study had only 24 participants. The most common side effect of transdermal delivery was local skin reaction in 8%.

β3-Adrenergic Receptor Agonist

Mirabegron is a β3-adrenergic agonist, which acts to relax the bladder during filling and has similar efficacy to anticholinergics in treatment of idiopathic overactive bladder [7]. In a recent study, patients with MS or SCI were randomized to placebo or 50 mg of mirabegron. The treatment arm had improvements in urodynamic and patient reported outcomes compared to placebo groups with a very low adverse event rate of only 3%. This low adverse event rate is very attractive

compared to the relatively high rate of adverse events with anticholinergic drug treatments. Another smaller study did not show similar improvements in objective urodynamic parameters, but did show significant decreases in patient symptom burden [8].

Combination Therapy

The combination of anticholinergics and β3-adrenergic agonists for treatment of idiopathic overactive bladder has been investigated in two recent trials (the SYMPHONY and SYNERGY trials) [9, 10]. Both trials demonstrated improved response of patients treated with mirabegron in combination with solifenacin at different doses when compared to monotherapy with solifenacin alone. The results were unclear about whether there was any benefit to combination therapy compared to monotherapy with mirabegron alone. There are limited data on the use of combination therapy with anticholinergics and β3-adrenergic agonists in patients with NLTUD.

Anticholinergics can also be combined with other medicines known to also affect bladder pressures. In one study, patients treated with anticholinergics alone with continued evidence of poor compliance had tamsulosin and imipramine added [11]. Tamsulosin is an alpha-adrenergic antagonist that is typically used in patients with benign prostatic hyperplasia, in order to decrease bladder outlet resistance. Alpha-adrenergic receptors, however, may have more widespread effects in the bladder, especially in the changes to the bladder urothelium and muscle associated with neurologic injury or disease. Imipramine is a tricyclic antidepressant, which has known effects on bladder pressure and activity. In this study, patients who were on anticholinergics had the addition of both drugs (triple therapy). These patients had urodynamics before (on anticholinergics alone) and after initiation of triple drug therapy. The patients' urodynamic assessments demonstrated decreased pressure at maximum capacity as well as dramatic improvements in bladder compliance. Use of combination therapy with these drugs may only be relevant for a few patients today, given the widespread availability of onabotulinum toxin (BTX); however, using these drugs to augment the effect of anticholinergics may be helpful for patients who cannot get BTX or develop immunity to the therapy.

Key Points: Medical Therapy

- There is no effective medical therapy to augment voiding phase dysfunction.
- Anticholinergics block receptors for acetylcholine at the motor endplate and are the mainstay of treatment for NLUTD.
- β3-adrenergic agonists (mirabegron) is a new class of medicine that has some developing evidence for treatment of NLUTD.
- Combination therapy with older medicines or possibly β3-adrenergic agonists may augment the positive effects of anticholinergics on the bladder.

Indwelling Catheters

Indwelling catheter consists of either a Foley catheter, which is placed via the urethra or a suprapubic cystostomy. A suprapubic cystostomy, commonly referred to as a suprapubic tube (SPT), is the same catheter that is used in the urethra, but travels through the lower abdomen into the cephalad portion or "dome" of the bladder and drains the bladder like a siphon. Indwelling catheters are in the bladder all of the time and are typically changed once per month. Indwelling catheters can be a very simple arrangement for patients with NLUTD; however, they are associated with the greatest complications of any bladder management strategy.

Although not intuitive, indwelling catheters have the greatest risk for kidney obstruction and renal failure. One would naturally think that having a catheter at all the time would achieve very dependable drainage of the kidneys. In fact, indwelling catheters in individuals with SCI have a greater risk of proteinuria, renal insufficiency, renal failure, hydronephrosis, and urinary calculi [12]. One explanation for this apparent paradox is the reaction of the bladder to the constant irritant of the catheter. Patients with indwelling catheters are at higher risk for UTI and urosepsis [13, 14] and one sequelae of chronic cystitis is increased fibrosis within the bladder wall. This fibrosis may act to mechanically obstruct the drainage from the ureter acting similar to a ureteral stricture.

In addition to higher UTI rates and worse kidney drainage, catheters also are associated with higher rates of other SCI-related complications. In fact, in the Model Systems of SCI care, which consists of 26 hospital across the US pooling data in the National SCI database, patients with indwelling catheters had higher rates of all-cause hospitalization, longer hospitalizations, and a higher rate of decubitus ulcers [13].

Another concern related to NGB and indwelling catheters is increased cancer risk. In general, patients with NGB have increased risk of developing bladder cancer. This risk is low, but higher than the general population [15]. Cancer risk has been addressed after agumentation cystoplasty and there is little evidence augmentation cystoplasty increases any risk of bladder cancer over baseline increased risk in neurogenic bladder [16, 17]. Indeed, current guidelines do not recommend screening patients for bladder cancer after augmentation cystoplasty. Due to the chronic inflammation associated with indwelling catheters, many clinicians perform yearly cystoscopy after a decade of use. However, guidelines and systematic reviews have not found strong evidence for this practice [18–20]. Unfortunately, bladder cancer when it develops in patients with NGB is often aggressive and it is unclear if yearly surveillance would even be effective at detecting bladder cancer early and preventing death from bladder cancer [17]. Because of the aggressive nature of bladder cancer in NGB patients, we consider early cystectomy even in some case of low-grade bladder cancer where patients would not have an indication for cystectomy (Fig. 8.1); however, this is controversial and many treat bladder cancer in the NGB population, stage for stage, the same as non-NGB patients.

A common misconception among patients and the medical community is that SPTs have a decreased risk of infection compared to Foley catheters. This has not been demonstrated, and generally, the reasons for use of a SPT over a Foley catheter are to avoid urethral complications [21]. Since many patients with NGB do not have

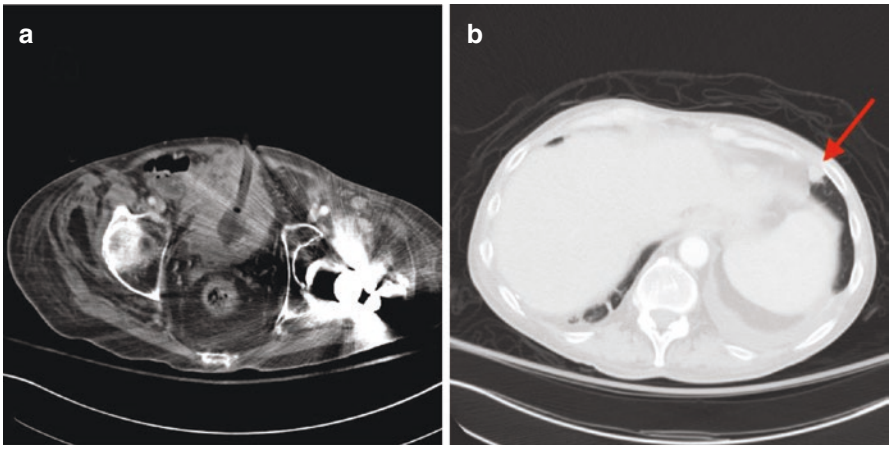

Fig. 8.1 (**a**) Large bladder tumor arising from suprapubic tube (**b**) metastatic pulmonary nodule at the time of presentation with bladder tumor. (With permission from Dr. Jeremy B. Myers)

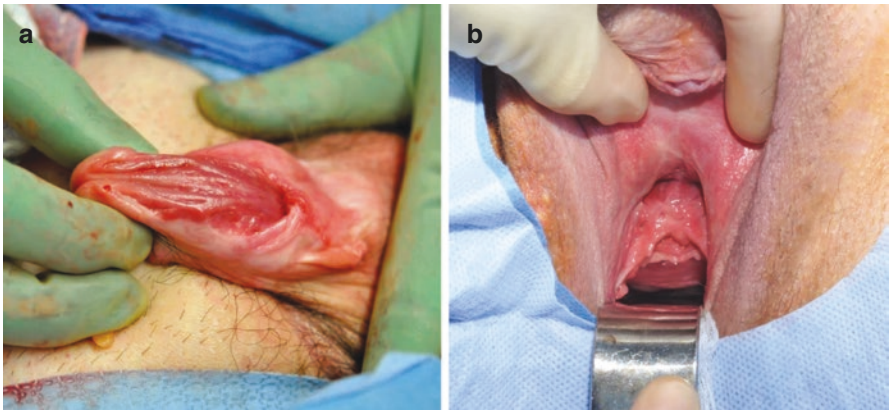

Fig. 8.2 (**a**) Ventral erosion of the penile urethra from pressure necrosis, (**b**) wide patulous erosion of the entire female urethra arising from a Foley catheter. (With permission from Dr. Jeremy B. Myers)

sensation in the bladder and urethra, they are prone to pressure-related complications from the indwelling catheter pulling against structures within the urethra. In men, this manifests itself as urethral erosion from the meatus to the penoscrotal junction by ventral pressure of a full urine bag dragging on the catheter (Fig. 8.2). Internally, in men, the catheter balloon causes pressure necrosis and pulls through the bladder neck into a cavity within the prostate or bulbar urethra. This can lead to incontinence and poor bladder drainage with hydronephrosis, UTIs, and even renal failure. In addition, once this problem is recognized and an alternative bladder drainage method is initiated, the urethral sphincters are no longer competent and patients will often have total incontinence from the urethra. In women, patients will have erosion of the bladder neck and sphincter, which usually manifests itself with catheters being pulled out inadvertently through the urethra with the balloon inflated. The first instinct for

care providers is to increase the size of the catheter or balloon of the catheter. This maneuver will work for a while, but eventually compounds the problem with worse pressure necrosis of the urinary sphincters. In addition, women can develop pubic symphysis fistulae and osteomyelitis from pressure necrosis of the bladder neck.

An SPT can be inserted in a small surgery or percutaneously and complications are rare. For the most part, insertion of an SPT will avoid these lower urinary tract complications and for this reason, most urologists recommend an SPT when patients plan on using indwelling catheters in the long term.

Key Points: Indwelling Catheters

- Indwelling catheters have the highest morbidity of any catheter-associated emptying.
- SPT may avoid urethral complications, which can cause serious morbidity from chronic indwelling Foley catheters.
- Despite increased morbidity, patient often favor indwelling catheters due to convenience and improved continence.

Onabotulinum Toxin Injection

The use of onabotulinum toxin (BTX) for treatment of NLUTD was approved by the Federal Drug Administration in 2011. There is strong level 1 evidence for BTX use in NGB for treatment of storage symptoms. The drug is administered by injecting the posterior wall of the bladder during a cystoscopy procedure (Fig. 8.3). Mostly, this is a short procedure done with local anesthesia in the clinic

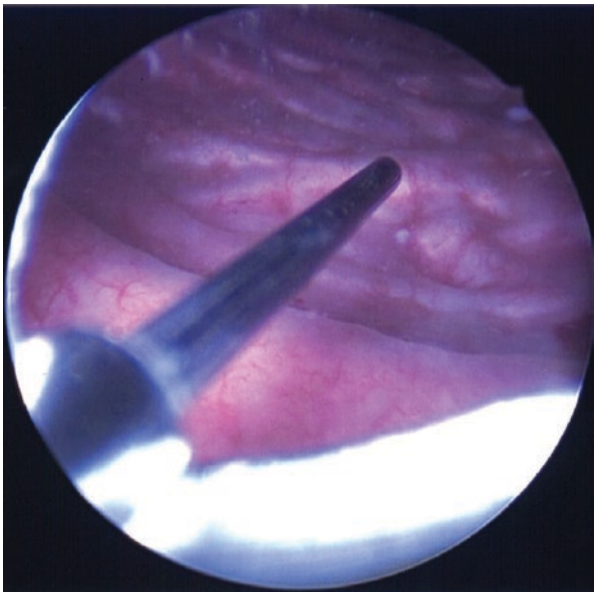

Fig. 8.3 Intravesical injection of botulinum toxin into the bladder wall with the aid of cystoscopy. The procedure takes about 5 min and most often is tolerated in the office with local anesthesia. (With permission from Dr. Jeremy B. Myers)

setting. Complications of the procedure include bleeding, patient discomfort, and urinary tract infection; rarely is the drug associated with systemic weakness [22]. Botulinum toxin, fortunately, works for a longer duration in smooth muscle, compared to skeletal muscle, and on average, it is injected about every 6 months into the bladder wall.

Two large studies, with essentially identical designs, randomized patients with either multiple sclerosis (MS) or spinal cord injury (SCI) to receive injection of placebo, 200 units, or 300 units of BTX [23, 24]. Outcomes of these studies were the change in number of incontinence episodes per week, urodynamic-based parameters (maximum cystometric capacity, maximum detrusor pressure during the first involuntary bladder contraction), and change in patient-reported quality of life. The results of these studies were dramatically positive in favor of injection of BTX over placebo. Patients had a decrease of 67–74% in number of urinary incontinence episodes (translating to about 20–25 less episodes per week), increased the maximum cystometric capacity by 150–160 ml, and decreased the pressures associated with involuntary bladder contractions. Patient-reported outcome measures included the Incontinence Quality of Life Questionnaire, which was also improved in the BTX groups compared to placebo [23, 24]. The studies also showed that there was no additional benefit to the use of 300 units over the results obtained with 200 units of BTX injection.

An additional meta-analysis was recently performed on individuals with SCI being injected with bladder BTX A [25]. Overall, the pre-BTX rate of incontinence, in the 734 pooled patients, was 23%, which was reduced to 1.3% after the use of BTX. In addition, the number of catheterizations per day and urodynamic assessed bladder pressures were also reduced with BTX injection.

Additionally, patients who respond to the initial botulinum toxin injection typically continue to respond and do not often develop resistance to the effect of injection [26]. In an extension of one of randomized studies mentioned above, there was a very low dropout rate over the 4 years of the study extension for adverse events (3%) or lack of efficacy (2%) [27]. It needs to be kept in mind that these are patients who responded to the therapy and requested retreatment and continuation of the study. Thus, they represent a population with inherent selection bias for positive response to BTX. When a patient has extensive fibrosis and bladder contraction, BTX injection is unlikely to be effective.

Key Points: Onabotulinum Toxin Injection

- There is good level 1 evidence that BTX injection can resolve incontinence, improve QoL and dramatically improve urodynamic parameters of bladder storage.
- BTX injection can mostly be given in the office, rarely has systemic side effects and most often can be used as long-term therapy.

Surgical Management

Bladder Augmentation

In bladder augmentation surgery, the bladder is opened and a patch of bowel is sewn onto the edges of the bladder expanding its volume and defunctionalizing the ability of the bladder to create coordinated spasticity. This surgery is also referred to as an enterocystoplasty because of the use of bowel to expand the bladder. Multiple bowel segments can be used in this surgery including small bowel, cecum and ascending colon, as well as sigmoid colon. In the past, stomach had also been used for enterocystoplasty; however, this was associated with hematuria and bladder-related complications.

Bladder augmentation has been demonstrated to have profound impact on bladder dynamics. When patients were assessed at an average follow up of 8 years, they were found to have substantial changes in urodynamics compared to their pre-augmentation urodynamics [28]. In one study, the mean bladder capacity increased from 200 cc to 615 cc, and the maximum detrusor pressure decreased from 81 to 20 cm H_2O. In this study, of the 26 patients only two continued anticholinergics and all but one patient had resolution or near resolution of incontinence. Bladder augmentation is also associated with the lowest patient-reported bladder symptoms and highest satisfaction when compared to those performing intermittent catheterization without augmentation or those who did CIC and had BTX injections [29]. This may be due to the profound change that occurs in the ability to store urine at low pressures.

The surgery can also be used to create an alternative channel to catheterize. This may be suitable for some patients that have urethral problems preventing catheterization, such as urethral strictures, false passages, and pain with passing the catheter. In addition, a catheterizable channel can help when patients lack adequate fine motor function or the strength and body habitus to position oneself in order to catheterize the urethra [30]. Usually, the catheterizable channel is also created from bowel segments, such as the appendix (called a Mitrofanoff), narrowed small bowel (Monti-Yang), or plicated terminal ileum (Fig. 8.4). These channels can come to the skin of the abdominal wall or to the base of the umbilicus where they form a small stoma that can be catheterized in a similar fashion to performing intermittent catheterization of the urethra.

Unfortunately, augmentation cystoplasty is a complex procedure that has significant peri-operative morbidity [30] and a high long-term revision rate. Both single center series and population-based analyses show that 34–46% of patients will need additional urologic interventions in the future, such as stone surgeries [28, 31, 32]. When patients are highly motivated to continue intermittent catheterization and have too much bladder fibrosis to respond to BTX injection or are not able to perform intermittent catheterization due to some of the reasons mentioned above,

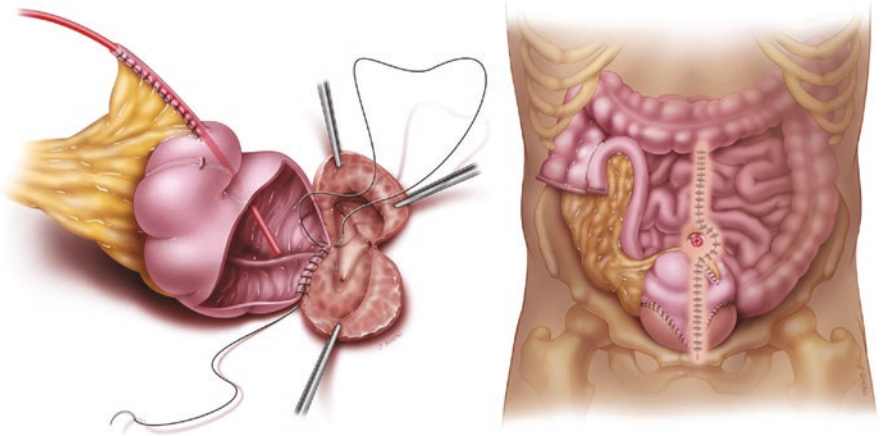

Fig. 8.4 Bladder augmentation with cecum, ascending colon, and creation of a catheterizable channel from plicated terminal ileum that makes a small stoma in the umbilicus to facilitate catheterization. (With permission from Dr. Jeremy B. Myers)

bladder augmentation with or without a catheterizable channel can preserve excellent bladder-related QoL. Patients just need to have a clear understanding of the potential for short- and long-term morbidity associated with the procedure.

Urinary Diversion

Conduit Urinary Diversion

Urinary diversion surgery involves the complete bypass of the bladder. Usually, urinary diversion consists of constructing a noncontinent urinary stoma out of bowel. The bowel segment connects internally to the ureters, which are disconnected from the bladder. The bowel segment is isolated from the fecal stream and the isolated segment is used as a "conduit" for urine from the kidneys and ureters to outside of the body. Most often, ileum is used to create the conduit, and the urinary conduit is referred to as an "ileal conduit." Many patients and practitioners also refer to urinary conduits as "stomas" or as a "urostomy." Both colonic and small bowel segments can be used to construct a urinary conduit. The reason that a portion of bowel must be utilized for this purpose rather than bringing the ureters directly to the skin is that cutaneous uretersotomies rarely stay patient in the long-term and are very prone to stenosis. Also, ureters tend to make a flat stoma, and for the urinary appliance or stoma bag, to fit over the stoma without leakage, the bowel has to have a nipple-like construction which projects from the abdominal wall 2–3 cm.

The most appropriate patients for urinary conduit construction are those who cannot or do not want to catheterize and do not tolerate an indwelling catheter. Often patients with tetraplegia or limited hand function will be treated with an indwelling catheter and chronic UTIs, urosepsis, or clogging of the catheter will necessitate

creation of a urinary conduit. From a patient perspective, there may not be much difference between an indwelling catheter and a "stoma," as both involve external bags for collection of urine. It is most often the complications from indwelling catheters that drive the decision for an incontinent urinary diversion.

Continent Catheterizable Pouch

Another type of urinary diversion, which can be used in NGB patients, is referred to as a continent catheterizable pouch. This surgery involves creation of a spherical bladder, made completely out of bowel. Rather than connecting to the urethra in the pelvis, this bladder is emptied with an intermittent catheter via a small stoma in the umbilicus or abdominal wall. Very often, this new bladder or "pouch" is made from the cecum and ascending colon. The channel that allows catheterization is made up of 8–10 cm of the tapered terminal ileum. This portion of the ileum is narrowed to about the same diameter of a pencil and the ileocecal valve is reinforced to prevent incontinence between catheterizations. This particular construction is referred to as a right colon pouch and arguably, the most common of these is the "Indiana Pouch" named after the institution where it was first described in the 1980s [33, 34]. The volumes of a right colon pouch are usually sufficient that patients catheterize four times daily to empty the pouch. Urinary diversion with a right colon pouch is an alternative to augmentation cystoplasty if the bladder has to be removed, such as in bladder cancer, fistula, and severe infection, or chronic debilitating pain. In these circumstances, preserving the remaining bladder, urethra, and native vesico-ureteral connections would not be possible, which are the main advantages of bladder augmentation cystoplasty rather than urinary diversion with a right colon pouch.

Neobladder

After removal of the bladder due to bladder cancer, a new spherical bladder constructed of bowel can be affixed to the urethral stump in the pelvis and patients void normally via the urethra. This arrangement is referred to as an orthotopic neobladder. However, in patients with neurologic disease this arrangement is rarely a solution, because function of the neobladder depends upon voluntary relaxation of the urinary sphincters and Valsalva voiding. Due to the neurologic dysfunction, patients who need urinary diversion, most often would not be able to coordinate sphincter relaxation and achieve spontaneous voiding. The neobladder can be emptied via intermittent catheterization via the urethra, but if intermittent catheterization is planned postoperatively, patients would likely just have an augmentation cystoplasty. Augmentation cystoplasty, compared to a neobladder, has the advantages of mitigating any risk of ureteral stenosis due to preservation of the natural connection at the vesico-ureteral anastomosis, and also allowing for less bowel to be used as the bladder will add a lot of surface area and volume to the spherically reconfigured bladder. For these reasons, few surgeons would treat patients with NGB with orthotopic neobladder.

Very similar to bladder augmentation, urinary diversion carries a very high perioperative and long-term morbidity. The reported mortality rates with the surgery vary, but range between 4 and 11% [35, 36]. Long-term complication rates are also high and include problems such as, UTI, urinary calculi, ureteral stenosis, metabolic and vitamin derangements, bowel obstruction, and hernias [37, 38]. In addition, surgical revision for urinary diversion complications is often needed. For instance, up to 22% of men need revision surgery at 16 months of follow-up after urinary diversion for complications of prostate cancer radiation [35] and up to 69% of patients need some revision surgery after right colon pouch [36]. Despite these complications, these surgeries can preserve QoL and are essential in treating serious complications of neurogenic bladder.

Key Points: Surgery

- The decision to undergo surgery is complex and the short and long-term morbidity must be weighed carefully against the patient's goals and preservation of renal function.
- Augmentation cystoplasty is associated with excellent patient reported QoL when the goal is to preserve the ability to perform intermittent catheterization.
- Urinary diversion may be needed in cases of bladder cancer, severe bladder dysfunction, or when patients do not have adequate hand function to perform intermittent catheterization.

Summary

Common treatments for neurogenic bladder span the spectrum from simple medical therapy to surgery to bypass or reconstruct the bladder. These treatments represent a time continuum and are not discrete choices. Some of the treatments work for a while and then more invasive treatments are needed as the bladder changes over time or patients experience neurologic disease progression. Follow-up and regular monitoring with a urologist or clinician familiar with the NGB and all of the treatment options available is essential in order to avoid or minimize complications and preserve patients' QoL.

References

1. Gajewski JB, Drake MJ. Neurological lower urinary tract dysfunction essential terminology. Neurourol Urodyn. 2018;37(S6):S25–31.
2. Manchana T, Prasartsakulchai C. Bethanechol chloride for the prevention of bladder dysfunction after radical hysterectomy in gynecologic cancer patients: a randomized controlled trial study. Int J Gynecol Cancer. 2011;21(4):730–6.

3. Yamaguchi O. Antimuscarinics and overactive bladder: other mechanism of action. Neurourol Urodyn. 2010;29(1):112–5.
4. Hadiji N, et al. Are oxybutynin and trospium efficacious in the treatment of detrusor overactivity in spinal cord injury patients? Spinal Cord. 2014;52(9):701–5.
5. Amarenco G, et al. Solifenacin is effective and well tolerated in patients with neurogenic detrusor overactivity: results from the double-blind, randomized, active- and placebo-controlled SONIC urodynamic study. Neurourol Urodyn. 2017;36(2):414–21.
6. Kennelly MJ, et al. Efficacy and safety of oxybutynin transdermal system in spinal cord injury patients with neurogenic detrusor overactivity and incontinence: an open-label, dose-titration study. Urology. 2009;74(4):741–5.
7. Krhut J, et al. Efficacy and safety of mirabegron for the treatment of neurogenic detrusor overactivity-prospective, randomized, double-blind, placebo-controlled study. Neurourol Urodyn. 2018;37(7):2226–33.
8. Welk B, et al. A pilot randomized-controlled trial of the urodynamic efficacy of mirabegron for patients with neurogenic lower urinary tract dysfunction. Neurourol Urodyn. 2018;37(8):2810–7.
9. Abrams P, et al. Combination treatment with mirabegron and solifenacin in patients with overactive bladder: efficacy and safety results from a randomised, double-blind, dose-ranging, phase 2 study (Symphony). Eur Urol. 2015;67(3):577–88.
10. Herschorn S, et al. Efficacy and safety of combinations of mirabegron and solifenacin compared with monotherapy and placebo in patients with overactive bladder (SYNERGY study). BJU Int. 2017;120(4):562–75.
11. Cameron AP, et al. Combination drug therapy improves compliance of the neurogenic bladder. J Urol. 2009;182(3):1062–7.
12. Weld KJ, Dmochowski RR. Effect of bladder management on urological complications in spinal cord injured patients. J Urol. 2000;163(3):768–72.
13. Cameron AP, et al. Medical and psychosocial complications associated with method of bladder management after traumatic spinal cord injury. Arch Phys Med Rehabil. 2011;92(3):449–56.
14. Anderson CE, et al. Bladder emptying method is the primary determinant of urinary tract infections in patients with spinal cord injury: results from a prospective rehabilitation cohort study. BJU Int. 2019;123(2):342–52.
15. Husmann DA, Rathbun SR. Long-term follow up of enteric bladder augmentations: the risk for malignancy. J Pediatr Urol. 2008;4(5):381–5. discussion 386
16. Higuchi TT, Fox JA, Husmann DA. Annual endoscopy and urine cytology for the surveillance of bladder tumors after enterocystoplasty for congenital bladder anomalies. J Urol. 2011;186(5):1791–5.
17. Higuchi TT, et al. Augmentation cystoplasty and risk of neoplasia: fact, fiction and controversy. J Urol. 2010;184(6):2492–6.
18. Consortium for Spinal Cord M. Bladder management for adults with spinal cord injury: a clinical practice guideline for health-care providers. J Spinal Cord Med. 2006;29(5):527–73.
19. Welk B, et al. Bladder cancer in individuals with spinal cord injuries. Spinal Cord. 2013;51(7):516–21.
20. Kreydin E, et al. Surveillance and management of urologic complications after spinal cord injury. World J Urol. 2018;36(10):1545–53.
21. Katsumi HK, et al. Urethral versus suprapubic catheter: choosing the best bladder management for male spinal cord injury patients with indwelling catheters. Spinal Cord. 2010;48(4):325–9.
22. Wyndaele JJ, Van Dromme SA. Muscular weakness as side effect of botulinum toxin injection for neurogenic detrusor overactivity. Spinal Cord. 2002;40(11):599–600.
23. Cruz F, et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. Eur Urol. 2011;60(4):742–50.
24. Ginsberg D, et al. Phase 3 efficacy and tolerability study of onabotulinumtoxinA for urinary incontinence from neurogenic detrusor overactivity. J Urol. 2012;187(6):2131–9.

25. Mehta S, et al. Meta-analysis of botulinum toxin a detrusor injections in the treatment of neurogenic detrusor overactivity after spinal cord injury. Arch Phys Med Rehabil. 2013;94(8):1473–81.
26. Del Popolo G, et al. Neurogenic detrusor overactivity treated with english botulinum toxin a: 8-year experience of one single centre. Eur Urol. 2008;53(5):1013–9.
27. Kennelly M, et al. Efficacy and safety of onabotulinumtoxinA therapy are sustained over 4 years of treatment in patients with neurogenic detrusor overactivity: final results of a long-term extension study. Neurourol Urodyn. 2017;36(2):368–75.
28. Quek ML, Ginsberg DA. Long-term urodynamics followup of bladder augmentation for neurogenic bladder. J Urol. 2003;169(1):195–8.
29. Myers JB, et al. The effects of augmentation cystoplasty and botulinum toxin injection on patient-reported bladder function and quality of life among individuals with spinal cord injury performing clean intermittent catheterization. Neurourol Urodyn. 2019;38(1):285–94.
30. Redshaw JD, et al. Procedures needed to maintain functionality of adult continent catheterizable channels: a comparison of continent cutaneous ileal cecocystoplasty with tunneled catheterizable channels. J Urol. 2014;192(3):821–6.
31. Welk B, et al. Population based assessment of enterocystoplasty complications in adults. J Urol. 2012;188(2):464–9.
32. Metcalfe PD, et al. What is the need for additional bladder surgery after bladder augmentation in childhood? J Urol. 2006;176(4 Pt 2):1801–5. discussion 1805.
33. Rowland RG, Kropp BP. Evolution of the Indiana continent urinary reservoir. J Urol. 1994;152(6 Pt 2):2247–51.
34. Rowland RG, et al. Indiana continent urinary reservoir. J Urol. 1987;137(6):1136–9.
35. Bassett MR, et al. Urinary diversion for severe urinary adverse events of prostate radiation: results from a multi-institutional study. J Urol. 2017;197(3. Pt 1):744–50.
36. Myers JB, Lenherr SM. Perioperative and long-term surgical complications for the Indiana pouch and similar continent catheterizable urinary diversions. Curr Opin Urol. 2016;26(4):376–82.
37. Shimko MS, et al. Long-term complications of conduit urinary diversion. J Urol. 2011;185(2):562–7.
38. Madersbacher S, et al. Long-term outcome of ileal conduit diversion. J Urol. 2003;169(3):985–90.