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Chapter

Urologic Implications and Management in Spina Bifida

Adrián Gutiérrez-González, José Iván Robles-Torres and Daniel García-Sánchez

Abstract

Urological disorders, including urinary infections, incontinence, and renal failure, represent a significant source of morbidity and mortality in these patients. Long-term mortality is associated to urological causes in approximately 33%. In order to prevent this complications, urologic evaluation since early childhood must be done. The evaluation of the degree of damage to the urinary tract and the determination of the type of neurogenic bladder involved in the spina bifida spectrum will be the guideline for establishing therapeutic management, which can be from behavioral modifications, medical management, minimally invasive therapy and, as a last resort, surgery. In this chapter, we will discuss the wide spectrum of urologic implications, a brief reminder of urinary tract physiology and the pathological processes involved in spina bífida, as well as long-term complications. The diagnostic evaluation of urinary tract and the different therapeutic modalities according to the type of neurogenic bladder and age will be discussed.

Keywords: urology, urinary tract infections, chronic kidney failure, management, augmentation cystoplasty, intermittent bladder catheterization

1. Introduction

1.1 The bladder and manifestations associated with spina bifida

The abnormal development of the neural tube is considered the most common cause of neurogenic bladder dysfunction in children. Nearly all patients with myelomeningocele (over 90%) will have some type of bladder dysfunction (neurogenic bladder), and 30–40% of these children will develop some degree of renal disease as a long-term complication if treatment is not implemented at an early age in childhood. [1]

Depending on the severity of the fusion defect and its location, a variety of neurological deficits can be seen, with variable impact on somatic, parasympathetic and sympathetic innervation of the bladder. For unclear reasons, the level of the lesion correlates poorly with urodynamics findings and the severity of lower urinary tract dysfunction. [2] This affects its ability to store and empty urine and can lead to chronic kidney disease by poor bladder dynamics. Urological problems, including urinary tract infections, incontinence, and renal failure, are a significant cause of morbidity and mortality. Long term mortality is associated to urological complications in approximately 33% of these patients. [3]

Children with myelomeningocele also have increased risk of developing kidney stones. In one study, the prevalence of kidney stones was 4 percent among children with spinal dysraphism, compared with 0.2 percent in healthy children. Likely mechanisms for this predisposition to upper tract urolithiasis include immobility (with resultant bone resorption), bacteriuria, and urinary stasis. [4]

The bladder is a hollow muscular organ whose function is to store urine to about 400–500 mL in adults and to void as a consequence of a consequence of a filling stimulus. The micturition cycle is the continuous event of storing and voiding of urine. Normal micturition lasts approximately 15–20 seconds, and typically the bladder empties seven times a day and, usually, never at night. Under normal conditions, the bladder works at low pressures constantly. That means that during filling phase, its pressure does not exceed 10 cmH20. This condition allows the continuous gravitational flow of urine from the ureter to the bladder, and not vice versa. When, for abnormal conditions, the pressure in the bladder exceeds 40 cmH20, urine flow stops and flows back to the ureters, causing their dilatation, and in the long term alteration of kidney function, culminating in end-stage chronic kidney disease if not treated promptly. Chronic kidney disease is one of the most frequent causes of mortality in patients with spina bifida. [5]

After surgical management, walking with or without aids can be achieved in all patients with sacral levels and 95% with low lumbar lesions, while lower urinary tract (LUT) dysfunction tends to remain as large post-void residual volume, high voiding pressures, and urinary incontinence. In contrast, in patients with occult spina bifida, most cases are incidentally found during X-ray screening of low back pain. The vast majority is asymptomatic. Some cases are accompanied by lipomeningomyelocele, dermoid cyst, or thick flum terminale with minimum skin changes such as a dimple and focal hypertrichosis. In this scenario, LUT dysfunction may present in late childhood or in adulthood, and the severity of symptoms can vary, from nocturnal enuresis to urinary retention. In other words, the impact of the LUT will depend on the type of spinal dysraphism, whether it is a cystic or it is limited to an occult presentation.

The pattern of dysfunction caused by spinal dysraphism is determined by the site and type of lesion. Patterns are divided in three regions: the region above the pons, the region between the pons and the sacral cord, and the sacral cord and infrasacral region. Each region has particularities in bladder function. It is important to clarify that the manifestations according to this classification are not exact in all cases. The presentation of the neurogenic bladder in spina bifida is unpredictable. The clinical manifestations tend to present great heterogeneity. These mixed lesions can occur especially with lesions in close proximity of the conus medullaris. [6]

A detailed description of the most frequent sites affected by spina bifida are explained below:

1.2 Infrapontine-suprasacral lesions

A spinal cord lesion above the lumbosacral level, depending on completeness of the lesion, may eliminate (complete lesions) or at least reduce (incomplete lesions) voluntary cerebral control of micturition leading to neurogenic detrusor overactivity mediated by spinal reflex pathways. Detrusor overactivity has important clinical implications: reduced bladder capacity, detrusor-sphincter dyssynergia with post-void residual urine, incontinence, and a high intravesical pressure, which translates to a higher risk for chronic kidney disease. Severity of the clinical

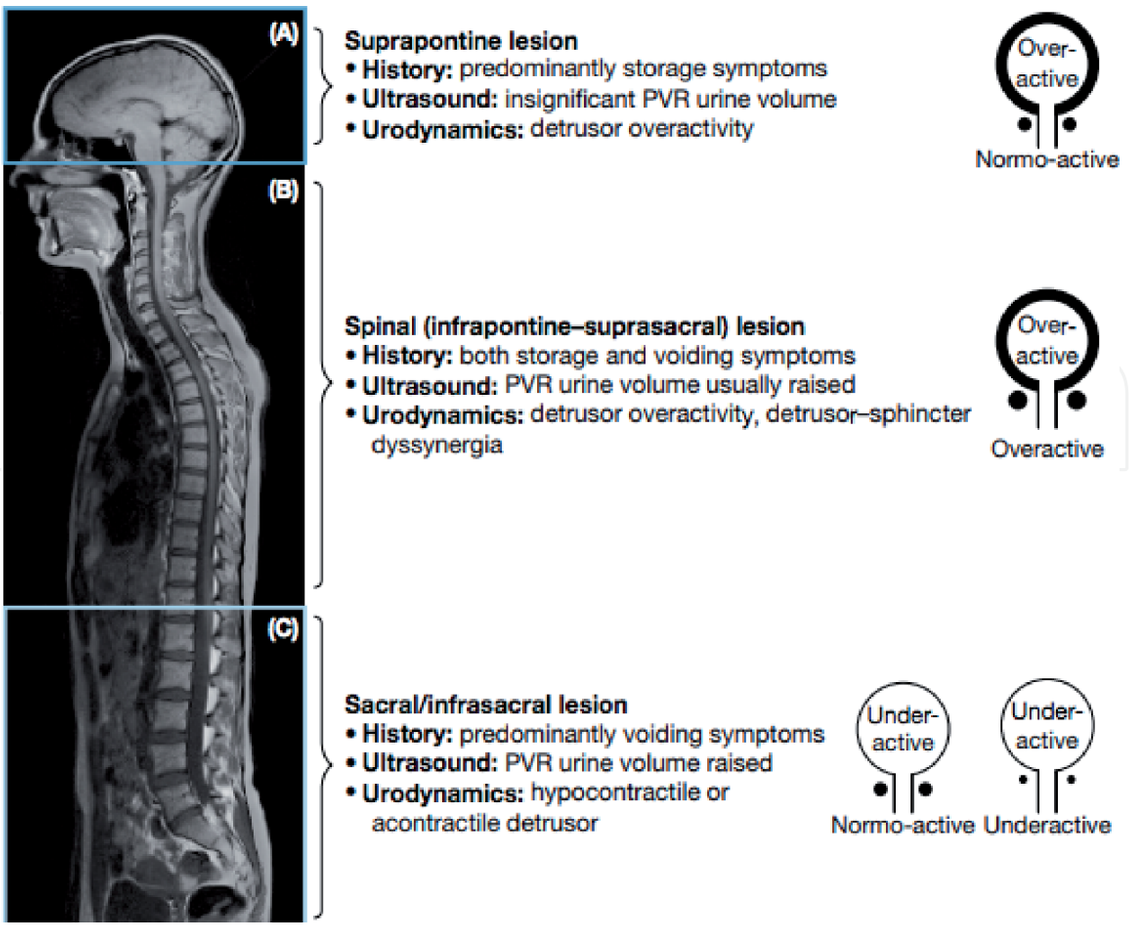


Figure 1.
Patterns of bladder dysfunction caused by neurological disorders: (A) Suprapontine lesion pattern; (B) Infrapontine-suprasacral pattern; (C) Sacral/infrasacral lesion pattern.

manifestations will depend on a complete injury is present and the level of injury (the higher, the more aggressive).

1.3 Sacral-infrasacral lesions

Lesions in this site will have predominantly voiding symptoms related to a hypocontractile (if incomplete lesion is present) or acontractile detrusor (complete lesion). The clinical presentation is due to injury to the parasympathetic motor nuclei that innervates the detrusor muscle. Stress urinary incontinence is usually related to Onuf's nucleus injury and pudendal nerve dysfunction over the striated sphincter (**Figure 1**).

2. Management of bladder storage and voiding symptoms

Lower urinary tract manifestations are divided into two groups: storage and voiding symptoms. Storage symptoms appear as an alteration in the filling phase of the micturition cycle. These symptoms include: increased voiding frequency, urgency, nocturia, urinary incontinence, and painful bladder syndrome.

Voiding symptoms appear as a difficulty during urination or prior to the onset of it. They include: difficulty to initiate urination, need to strain or effort to initiate and maintain urination, weak or intermittent urinary stream, terminal drip, dysuria and urgency. These symptoms result in incomplete voiding.

The primary goal of treatment is to preserve upper urinary tract function, improve continence, and improve quality of life in these patients. [5]

2.1 Storage management

In the scenario of the neurogenic patient associated with spinal dysraphism, the main complaint reported by patients is urinary incontinence, accompanied or not by urinary infections. Urinary incontinence can be explained by several pathophysiological mechanisms. Urodynamics is a useful tool that provides objective diagnostic information that allows us to know the specific cause of incontinence.

Treatment includes behavioral measures such as control of fluid intake and personal hygiene. The use of medications should always be combined with conservative measures. The aim of these drugs is to increase bladder capacity and decrease detrusor pressure. Anticholinergics (also named antimuscarinics) are the most commonly used drugs. Its efficacy has been demonstrated in neurogenic patients with urge urinary incontinence associated with an overactive detrusor. Beta 3 agonists are another option that was recently introduced. The efficacy of these drugs appears to be similar to anticholinergics with a non-inferior safety profile. The response to these medications is evaluated with the clinical control of incontinence, as well as an improvement in bladder capacity objectively observed by a decrease in detrusor pressure of less than 40 cmH2O when having a maximum bladder capacity in urodynamics. [5, 6]

2.2 Voiding symptoms

These patients are at a higher risk of presenting high filling pressures, which generates vesicoureteral reflux, resulting in dilatation of the upper urinary tract and deterioration of renal function. Chronic retention and reflux to the upper tract are conditions that increase the risk of urinary infections. Management focuses on improving and maintaining detrusor pressure below 40 cmH2O and control of urinary incontinence.

The use of clean intermittent catheterization as a mechanism for bladder emptying is considered the treatment of choice in the vast majority of neurogenic patients with evidence of urine retention. This treatment aims to adequately empty the bladder and thereby reduce urinary infections and incontinence. The use of an indwelling transurethral or suprapubic catheter should be avoided due to the demonstrated risks of recurrent urinary tract infections, stone formation, and urethral trauma [6] (**Figure 2**).

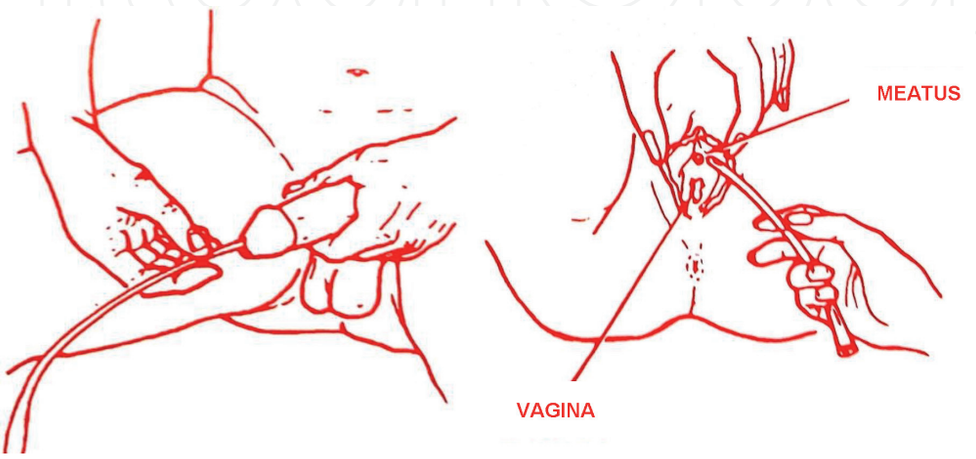


Figure 2.
Clean intermittent catheterization technique in male and female.

In patients where a functional voiding alteration is confirmed with dysfunction of the relaxation of the sphincter in the emptying phase of the micturition cycle, they can benefit from physiotherapy and biofeedback, which consist of training to improve bladder-sphincter coordination during urination. [5]

3. Follow-up protocol according to age

The main priority at the moment of birth is the closure of the spinal defect, as neurological complications are the main cause of morbidity and mortality during the first year of life; followed by urological complications. Specialized treatment centers state that the urological management should start immediately with intermittent catheterizations and anticholinergic medications due to the risk of collagen deposition in the bladder wall and consequent increased risk of upper urinary tract damage. In fact, each of the steps toward the management of this congenital disease are complex and the decisions may vary. [7]

3.1 Management from the moment of birth to the age of two years

A sonographic evaluation of the upper urinary tract as well as urine cultures are performed every 3 to 4 months. If both tests are normal, we wait until the age of 2 years, the age expected for most children to achieve voluntary control of micturition. In case of abnormal findings during any of the sonographic evaluations or 3 or more positive cultures accompanied with symptomatic infections during a year or less are encountered, it would be necessary to perform urodynamic testing complemented with a cystogram to discard any possibility of upper urinary tract damage due to a hostile bladder. If this is the case, it is time to start the adequate anticholinergic treatment and intermittent catheterizations. [8]

If no abnormal findings during this first 2-year follow-up are seen, an expectant management may be allowed.

3.2 Management from the age of two years to 20 years

Expectant management is modified to active management. Treatment goals are as follows: a) Avoidance of renal damage, b) Preservation of continence and c) Treatment of symptomatic urinary infections.

The first step is the functional evaluation by urodynamics and a structural evaluation with a cystogram. Videourodynamics is the Gold Standard as they are capable of evaluating both parameters. [9] A family member should be trained to perform clean intermittent catheterizations, so when the patient reaches the age of 6 years, this information should be passed onto the child to start self-intermittent catheterizations. We conducted a clinical trial in which we observed that intermittent catheterizations with clean technique using re-sterilized catheters did not increase neither the risk of urinary tract infection, nor bladder bacterial colonization. [10]

By performing urodynamic tests, the type of functional disturbance of the bladder may be assessed and classified in 4 types according to the Madersbacher classification: [11].

Type 1: High bladder pressure. High sphincter pressure.
Type 2: High bladder pressure. Low sphincter pressure.
Type 3: Low bladder pressure. High sphincter pressure.
Type 4: Low bladder pressure. Low sphincter pressure.

The risk of upper urinary tract damage is higher when Madersbacher type 1 and type 3 bladders are encountered. After identification of the bladder type, anticholinergic treatment should be started to normalize increased pressures. Three months after beginning of treatment, follow-up with a new urodynamic test is performed to assess the improvement of urodynamic parameters and clinical status.

The morphology of the bladder and the presence of vesicoureteral reflux (VUR) are assessed with a cystogram. The risk of vesicoureteral reflux in patients with neurogenic bladder is up to 17%. When VUR is observed, it is important to measure the detrusor pressure; if a pressure greater than 40 cmH20 is found, before thinking of any surgical treatment such as ureteral reimplantation, an attempt is made to decrease these pressures with conservative treatment. In case of success, a new evaluation is made to reassess if RUV disappeared (**Figure 3**) [12].

After functional and structural evaluation, proper bladder classification and having started initial treatment, the second stage of management is continued. Follow-up is made with urine cultures every 3 months, renal sonography every 6 months and renography every 1 to 3 years. Regarding the urodynamic test, when the detrusor pressure is greater than 40 cmH2O, the medical treatment is modified and a new urodynamic test is performed 3 months after, this is done until the goal of detrusor pressure of less than 40 cmH2O is achieved [13].

When to perform a new urodynamic test? 1) When there is less than 90% of voluntary micturition control. 2) When a new morphologic or functional disturbance of the kidney is observed. 3) Five years after the last urodynamic study. During this time, the type of neurogenic bladder could be modified due to the morphologic changes of growth and its effect on spinal cord. [14]

3.3 Management from the age of 21 years and over

When entering this stage, the patient is more aware of the disease and is more organized in its management. The bladder type usually reaches a stable state, and it is uncommon for the neurogenic bladder type to change. If this happens, it is important to evaluate the possibility of having a neurological disturbance that could need primary treatment.

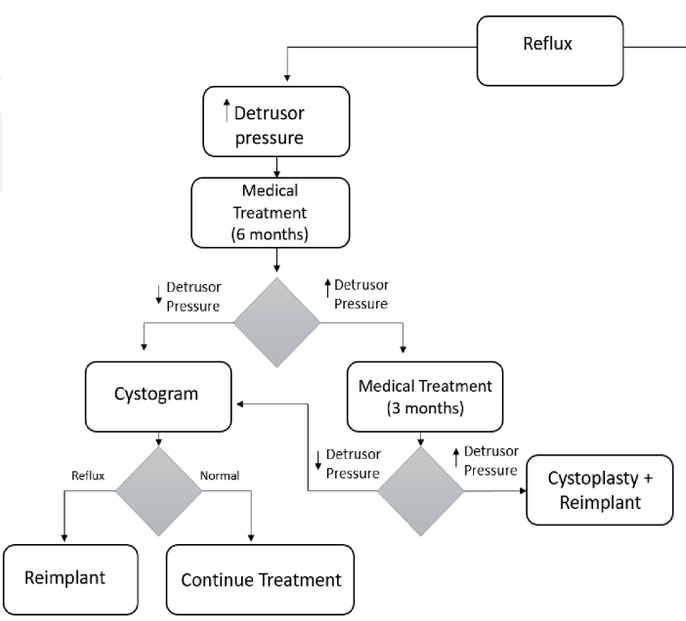


Figure 3.
Diagnostic and therapeutic algorithm in neurogenic bladder with vesico-ureteral reflux.

By this age, intermittent catheterizations are usually mastered by the patient and clinical signs that could be suspicious of active infection are well identified. Other topics, such as sexuality and reproduction are approached. Reproduction methods are informed and instructed; recommendations are given to women who wish to reproduce, such as folic acid intake and modifications on the route of administration of oxybutynin, from the oral to the intravesical route. [15]

On November 23rd of 1993, we founded the Spina Bifida Association in Moterrey, Mexico, where we presently have 1055 patients enrolled with the following age ranges:

< 15 years: 311 (29.5%)
16–29 years: 572 (54.2%)
>30 years 172 (16.3%)
Total: 1055 (100%)

A total of 472 (44.7%) patients assist with relative frequency (At least 3 consultations per year). Our experience has been forged working with the everyday management of our patients during 26 years, assessing their progression and deciding which procedures are the most adequate for them.

4. Urinary tract infections, when to treat?

Patients with neurogenic bladder due to spinal dysraphism have several factors that potentially increase the risk of urinary tract infections, such as, vesico-ureteral reflux (any grade), hypertonic bladder and foreign bodies inside the bladder. Schlager et al. observed that 70% of patients that perform intermittent bladder catheterizations present asymptomatic bacteriuria 24 weeks after the beginning of treatment. [16]

In patients with neurogenic bladder, including those secondary to myelomeningocele, urinary tract infections should be considered differently from those without any neurofunctional disease. The presence of bacteriuria within this group of patients is very common and unnecessary antibiotic treatment could be given if there is no acknowledgment of these facts. This could lead to future complications that develop due to antibiotic resistance and antibiotic side effects.

In patients performing intermittent bladder catheterizations, urine culture results with more than 10,000 CFU/ml are considered a clinical infection only when one or more of the following clinical features are present: foul smell, cloudy urine, fever of 38°C or more and abdominal or flank pain. [17] Positive urine culture without other clinical features is considered as bacterial colonization and requires no antibiotic treatment.

When deciding which antibiotic to prescribe, it is important to consider which antibiotics show the highest resistance within a community, which option would be delivered at adequate concentrations to the urinary bladder, this depending on the kidney's capacity to eliminate the active drug, and which would be more suitable to eliminate infection. It is important to ponder these considerations before antibiotic administration, as damage to the renal parenchyma may develop in a kidney already vulnerable to damage. [18]

Among the behavioral methods that help us in the prevention of urinary tract infections we include: Adequate liquid intake, maintenance of low postvoid urine and short time periods between intermittent catheterizations.

Intermittent bladder catheterization is a risk factor that predisposes to infection. There is no significant difference in the prevention of urinary tract infections when comparing the sterile technique with the clean technique, as well as with the use

of a sterile catheter compared to a reused clean catheter; furthermore, the risk of colonization is the same between both techniques. [19]

5. Refractory cases to medical management

The objective of neurogenic bladder management secondary to myelomeningocele is focused on three main objectives: 1) Decrease the risk of renal damage 2) Preserve urinary continence and 3) Prevent urinary infection episodes. When these objectives are not reached with medical management, it is necessary to take more drastic decisions, otherwise, further problems regarding renal function may be encountered and quality of life may be affected. Such procedures include:

5.1 Neuromodulation

An attempt is made to modulate the nerve reflexes that control the bladder, sphincter and the pelvic floor through sacral nerve stimulation. The use of this technique is well documented in certain neurologically affected patients; however, in patients with myelomeningocele, there are controversial results due to structural abnormalities found at a sacral level, which makes this technique a lot harder. Evidence is still limited; however, this remains a continuous field of investigation (**Figure 4**) [20].

5.2 Augmentation cystoplasty

The aim of this procedure is to increase the bladder capacity and decrease elevated pressures in the urinary tract through an intestinal patch surgically fixed at the bladder dome. Some contraindications for these procedures are: 1) Any functional or structural disturbance of the gut, 2) Disturbances of hand dexterity to perform intermittent catheterizations, 3) Cognitive disturbances and 4) Significant damage to the renal function. [21] Significant changes have been observed after surgery regarding bladder storage as well as a decrease in filling pressure. Some early complications reported in the recent literature are wound infection (4–6%)

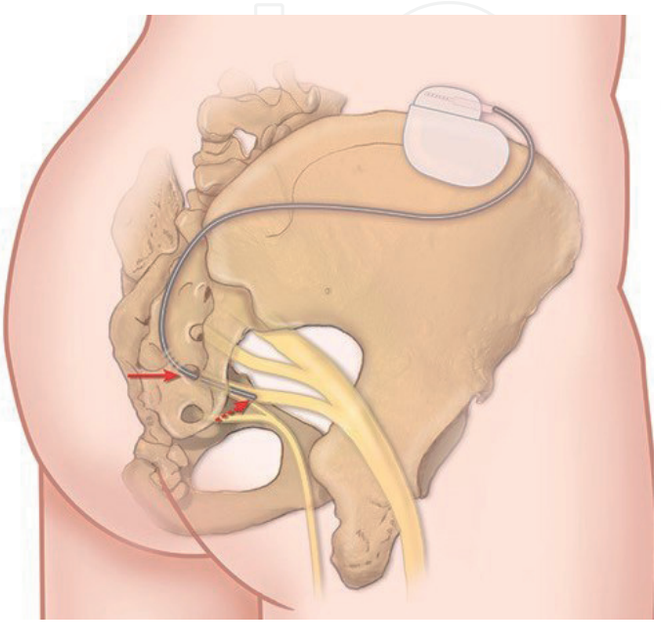


Figure 4.
Sacral neuromodulation therapy for refractory cases.

and intestinal obstruction (3–6%). The mortality rate within this group of patients is reported between 0 and 2.7%. Long-term complications include metabolic disturbances, such as hyperchloremia (16%) and decrease in renal function in patients with a creatinine clearance lower than 15 ml/min (15%) or higher than 40 ml/min (4.1%). [22] Mucus production by the intestinal lining is estimated between 35 and 40 gr/day, which predisposes to stone formation, infection and obstruction. After catheterizations, we perform intravesical irrigations with sodium bicarbonate at a dilution of 0.75% to reduce mucus thickness and attempt to reduce its production (**Figures** 5–7).

Perforation after bladder-gut anastomosis has been reported in 0.8–13% of procedures, occurring approximately 2 years after surgery, with a mortality rate of 25%. Risk of bladder cancer has been reported 10–20 years after surgery, and is believed to be caused by urinary stasis, nitrosamines, bladder stones, chronic inflammation of the intestinal patch and possible immune mechanisms with an estimated incidence of 10–20%. [23, 24]

Cystoscopy surveillance is recommended after a period of 10 years of surgery and in patients that develop hematuria, suprapubic pain or recurrent urinary tract infections.

5.3 Urinary diversion

Ileovesicostomy uses ileum as a bypass between the bladder and skin. This technique represents many clinical problems due to obstruction; furthermore, it predisposes to infections and bladder stones The Ileal conduit technique uses an

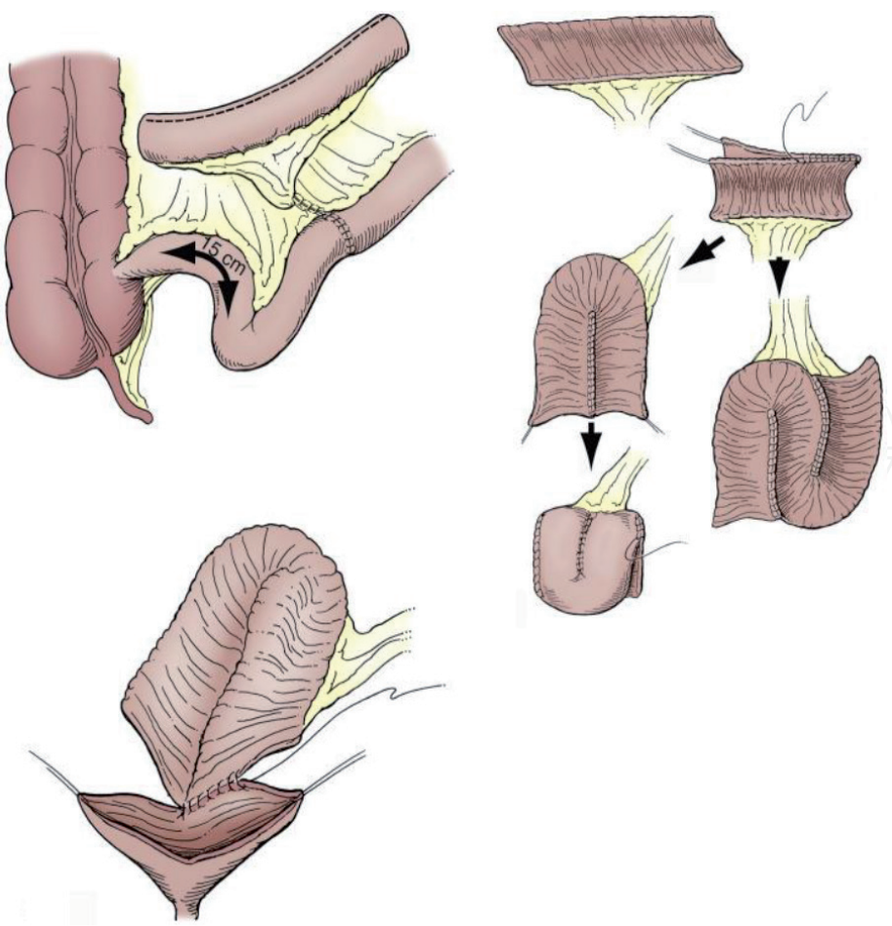


Figure 5.
Ileocistoplasty: a segment of ileum is remodeled and anastomosed to the bladder dome to increase the capacity of the bladder.



Figure 6.
Colocystoplasty: a segment of colon is remodeled and amastomosed to the bladder dome. Image obtain from hospital Universitario "Dr. José Eleuterio González", shared by Dr. Adrián Gutiérrez González.

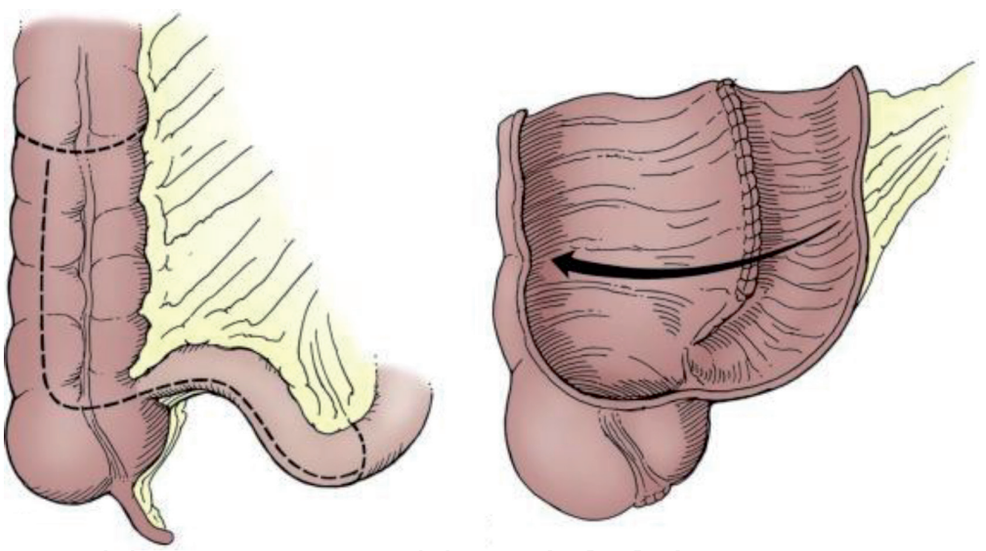


Figure 7.
Ileocecocystoplasty: Distal ileum and cecum are used to anastomose to the dome of the bladder.

ileum fragment which is closed at one end, both ureters are anastomosed to the conduit and the remaining open ileum end is connected to the abdominal wall, urine is collected by an external pouch. [25]

5.4 Catheter drainage

The permanent use of urinary catheters is not a good option due to the multiple complications that could develop. These include recurrent infections, meatal erosion, traumatic hypospadias, and stone formation. However, this technique can be used in cases with no other alternative options. If this were the case, the possibility of a suprapubic tube would be the most suitable option, which presents fewer complications. It is reserved only for patients with bladder emptying disturbances. This procedure is not recommended for patients with hyperactive neurogenic bladder, as urine leak surrounding the catheter entrance could appear. [26]

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