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Lesson 23 Volume 39

Contemporary Augmentation Cystoplasty*

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to describe the indications for augmentation cystoplasty and contemporary surgical techniques used to perform them. The participant will also be able to recognize complications of augmentation cystoplasty and describe how to manage these issues.

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***This AUA Update addresses the Core Curriculum topic of Neurogenic Bladder and the American Board of Urology Module on Neurogenic Bladder, Voiding Dysfunction, Female Urology, BPH and Urethral Stricture.**

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INTRODUCTION

Augmentation cystoplasty may be used in the treatment of refractory lower urinary tract disorders in both neurogenic and non-neurogenic cases. However, it is most commonly employed in patients with congenital or acquired neurogenic bladder, specifically those with spinal cord injury, multiple sclerosis or spinal dysraphism. The 2 primary goals for bladder management are 1) protecting the upper and lower urinary tract by maintaining a low pressure, compliant bladder and 2) improving quality of life, often by increasing continence and independence.[1] To accomplish these goals, a graduated approach is often used, moving from conservative to invasive management strategies.

Historically neurogenic bladder has been managed by clean intermittent catheterization as described by Lapides et al in 1972.[2] This approach revolutionized care of the neurogenic bladder as renal failure had previously been the most common cause of death in this population. The advent of antimuscarinic and beta3-agonist medications, neuromodulation and intravesical onabotulinumtoxinA injection has provided additional options for neurogenic and non-neurogenic bladder disorders. In fact, due to a rise in the use of intradetrusor onabotulinumtoxinA, between 2000 and 2010 performance of AC decreased by 38%.[3] When these measures fail to result in acceptable bladder pressures or continence, bladder augmentation should be considered.

In this Update we review the contemporary indications and surgical techniques for AC, and discuss how to recognize and manage complications. We also describe innovations and advancements in the field of AC.

INDICATIONS FOR AUGMENTATION CYSTOPLASTY

Patients with refractory lower urinary tract dysfunction or neurogenic bladder should be evaluated at least annually.[1, 4] Urodynamic monitoring, renal ultrasound, serum creatinine (or cystatin C when indicated) and patient reported outcome measures should be used to monitor subjective and objective parameters. The etiology of neurogenic bladder has an important role in the expected concomitant symptoms and natural history of both the bladder and the outlet. Careful evaluation with physical examination and history, including assessment of patient mobility and manual dexterity and social support, is crucial when discussing realistic and feasible treatment options.

The goal of augmentation cystoplasty is to increase the capacity, and hence compliance, of the bladder. AC is the gold standard for cases that have failed conservative management with anticholinergics or beta3-agonists, or intravesical injection of onabotulinumtoxinA and/or CIC.[4] Appendix 1 lists several pathological processes that can result in a decompensated bladder that may benefit from augmentation, as well as relative contraindications to bladder augmentation including circumstances that preclude use of bowel.[5]

SURGICAL TECHNIQUE

Augmentation cystoplasty involves addition of an enteric segment to the bladder with the goal of creating a low pressure, high volume reservoir and ultimately improving several characteristics including bladder compliance and capacity. Augmentation may also preserve renal function and improve incontinence that occurs secondary to detrusor overactivity.[4]

A variety of enteric segments have been used for AC, such as stomach, jejunum, ileum and colon, each with its own advantages and disadvantages, including mucus production, peristalsis and metabolic disturbances (Appendix 2). The general surgical approach is similar regardless of enteric segment and involves patching detubularized bowel to a bivalved bladder. A coronal or sagittal incision may be used to clamshell the bladder. It is important to **extend the incision widely in order to defunctionalize the bladder and prevent a narrow mouthed anastomosis, which would allow the augment to mimic a diverticulum.**[5] The bowel segment is opened along the antimesenteric border and reconfigured into a spherical shape, which maximizes surface area and therefore volume, and blunts bowel contractions.[4] Permanent sutures are avoided as they are a nidus for stone formation. A suprapubic tube is brought out of the native bladder anteriorly through the abdominal wall and an intraperitoneal drain is left in place.

Ileocystoplasty. **The most common bowel segment used is the ileum given its lower risk of metabolic derangements.** An ileal segment measuring approximately 20-40 cm is harvested a minimum of 15 cm proximal to the IC valve. The length of ileum harvested is dependent on the native bladder capacity and the age and size of the patient. **The segment to be used should have adequate mesentery to reach the native bladder tension-free.** We use a sagittal incision (from posterior to anterior bladder neck) to bivalve the bladder when using ileum, which allows for a tension-free anastomosis. The harvested segment is detubularized and most commonly configured into an inverted "U" prior to its anastomosis to the bladder, although "S" and "W" shapes have been described.

Sigmoid colocystoplasty. **The sigmoid colon is also frequently selected and is especially appropriate in patients with short ileal mesenteries or when use of small bowel is contraindicated**. Approximately 20 cm is typically required. The redundancy, especially in patients with neurogenic bowel and chronic constipation, makes it easy to position on the bladder. The sigmoid colon commonly has a large capacity and abundant mesentery, although it has attendant increased mucus production and higher end filling pressure secondary to colonic contractions.

Ileocecocystoplasty. When using the cecum, the right colon must be mobilized along the white line of Toldt up to the level of the hepatic flexure. Typically 15 to 30 cm terminal ileum is used, although the length of ileal segment depends on the technique used. We prefer a modified Indiana augmentation or continent catheterizable ileocecocystoplasty, which allows for use of the IC valve as a continence mechanism (fig. 1).[6-8] The appendix may be left intact or removed. Initially described by Sarosdy in 1992, in this procedure after the IC segment is harvested the right colon is opened longitudinally and anastomosed to the bivalved bladder, usually with a coronal incision

ABBREVIATIONS: AC (augmentation cystoplasty), CCC (cutaneous catheterizable channel), CIC (clean intermittent catheterization), IC (ileocecal), UTI (urinary tract infection), VUR (vesicoureteral reflux)

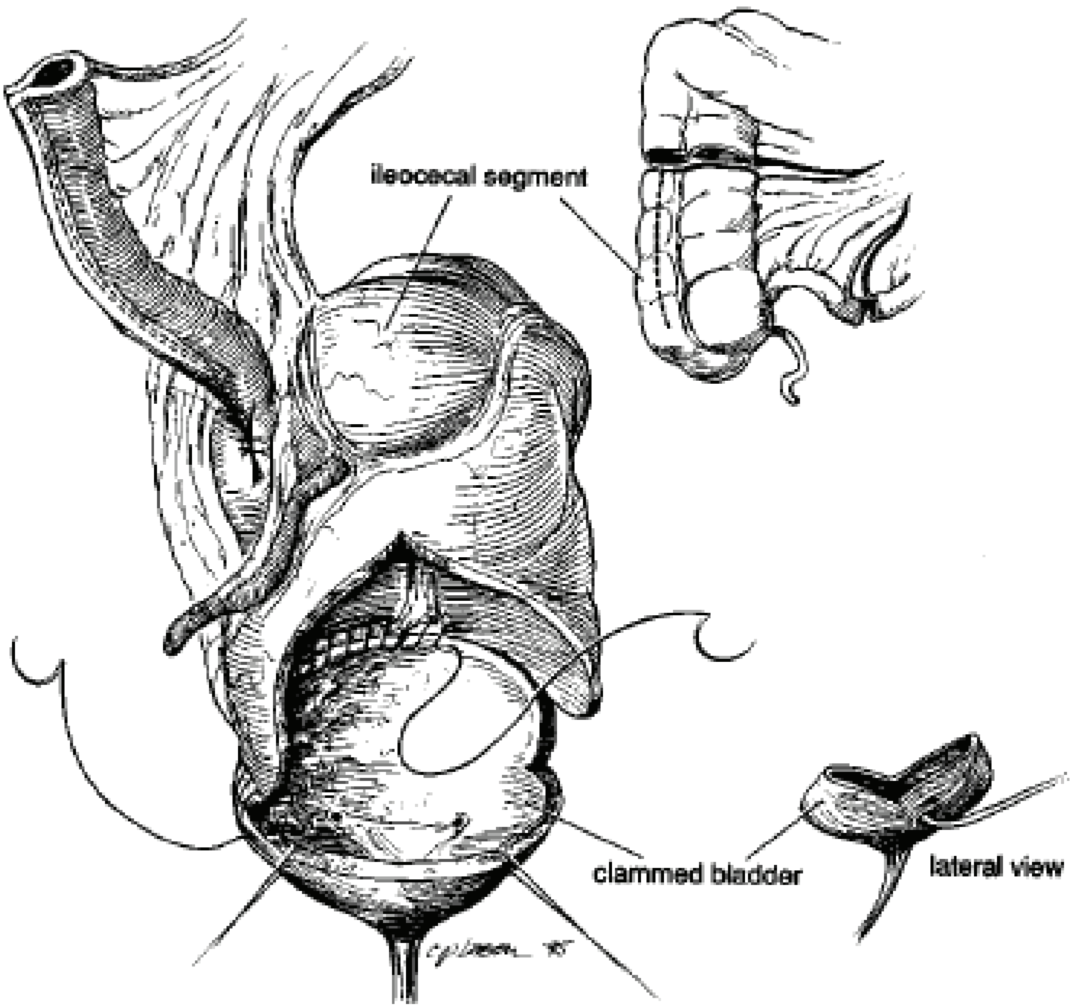

Figure 1. Diagram of ileocecocystoplasty with enteric segment anastomosed to clamshelled bladder.[7]

extending from one ureteral orifice to the other.[6] The channel is then created by tapering the ileal segment over a 14Fr catheter using a GIA™ 60 stapler. The valve is then imbricated further using non-absorbable sutures. **It is important to counsel patients that a competent IC valve is antirefluxing, and therefore resection of this valve may lead to diarrhea and/or malabsorption, although in neuropathic cases where neurogenic constipation coexists this potential complication can improve stool consistency and bowel movements.** Our review of the data revealed that no patients experienced chronic diarrhea (fig. 2).[8]

Gastrocystoplasty. In cases where alternative bowel segments are contraindicated gastrocystoplasty has been selected, which confers the benefits of less mucus production, decreased infection risk and reduced metabolic derangements. **Unfortunately hematuria-dysuria syndrome occurs in approximately 25% of patients and the risk of malignancy is as high as 10%.**[9] Given the high complication rate with use of stomach, this approach has largely fallen out of favor and is no longer recommended.

ALTERNATIVES TO ENTERIC SEGMENT

Autoaugmentation. First described by Cartwright in pediatric patients, autoaugmentation creates a low pressure bladder diverticulum by removing the detrusor from the urothelium, with the goal of increasing capacity and compliance.[10] Long-term outcomes have shown mixed results with anywhere from 10% to 50% of patients requiring subsequent enterocystoplasty. In patients with demonstrated efficacy over time a preoperative bladder capacity of more than 75% of expected capacity for age is an important predictor of success.

Ureterocystoplasty. Redundant ureter (eg from a congenital megaureter) is used in ureterocystoplasty. The ipsilateral kidney may be preserved with transureteroureterostomy, or nephrectomy may be performed if the kidney is non-functioning. Johal et al observed that in the majority of patients end fill bladder pressure and capacity are improved, although long-term results show as many as 24% of patients requiring enterocystoplasty due to poor compliance and high pressure.[11]

SPECIAL CONSIDERATIONS WITH AUGMENTATION CYSTOPLASTY

Continent cutaneous catheterizable channel. Patients with limited mobility, especially those in a wheelchair, may benefit from concomitant CCC to facilitate catheterization. Various techniques involving appendix (Mitrofanoff) and ileum (Yang-Monti) have been described. However, in adults the best outcomes have been achieved using tapered ileum with the modified Indiana augmentation.[12]

Bladder outlet procedures. Augmentation alone often

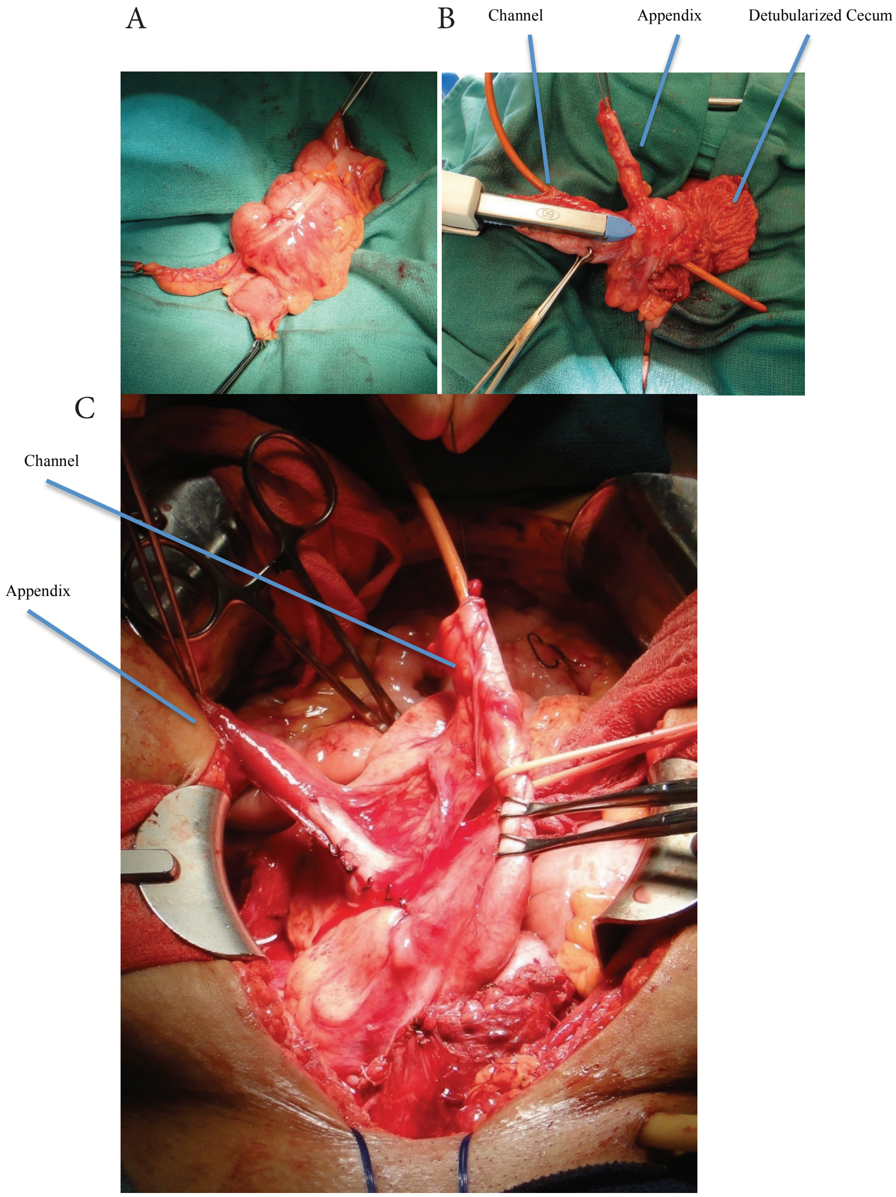

Figure 2. Intraoperative images of ileocecocystoplasty with continent catheterizable channel. *A*, cecal segment with terminal ileum and appendix. *B*, tapering catheterizable channel over catheter with stapler. *C*, plication sutures along catheterizable channel to reinforce continence mechanism.

improves or resolves urinary incontinence in patients with an incompetent outlet, and surgeons may therefore elect to stage an outlet procedure. If the incontinence is severe, a concomitant bladder outlet procedure may be performed. Injectable bulking agents, bladder neck reconstruction, bladder neck closure, synthetic or autologous slings and artificial urinary sphincters (bladder neck or bulbar cuffs with or without pumps) have been used, each with varied indications and success.[13, 14]

Ureteral reimplantation. VUR in neurogenic bladders may result from high pressure systems and therefore should improve or resolve with a reduction in intravesical pressure following AC. Zhang et al observed complete resolution of VUR in 83% of patients, improvement in 10% and no change in grade in 7%.[15] In contrast, when Wang and Liao examined data of 173 patients undergoing AC, of whom 160 underwent concomitant ureteral reimplantation, they found that patients with VUR at low pressures, ureterovesical junction obstruction or grade III or higher VUR benefited from reimplantation.[16]

Special considerations for women. Female patients with congenital genitourinary abnormalities may present earlier and with more severe pelvic organ prolapse. While minimal data have been published on long-term outcomes of prolapse repair in this population, concomitant hysterectomy and/or prolapse repair should be considered if the patient has completed childbearing.[17]

CONTEMPORARY OUTCOMES

Functional outcomes, while variable depending on the underlying preoperative bladder pathology and surgical technique used, have shown consistent, durable success with regard to continence, compliance, capacity and quality of life improvements.[18, 19] **In the contemporary literature overall continence**

rates range from 71% to 100%, regardless of underlying neurogenic etiology. However, patients may continue to require anticholinergics and/or CIC to stay dry.[18–20]

In 2017 Hoen et al systematically reviewed 20 studies including 511 patients undergoing AC for neurogenic bladder.[19] Given the lack of standardized patient reported outcome measures and follow-up in the neurogenic bladder population, there was little consistency in reporting across the 20 studies. **Still, the results indicated overall improved quality of life, stable renal function, and improved continence and urodynamic parameters.** Earlier studies had similar results with a significant improvement in bladder capacity and reduction in mean maximum detrusor pressure.[8, 18] Long-term data out to 10 years indicate that improvement in bladder compliance is sustained.[18, 21]

With regard to quality of life, Myers et al conducted a survey of 879 patients with neurogenic bladder who performed CIC, of whom 175 had previously undergone bladder augmentation.[22] Patients who underwent AC had few bladder management problems, better bladder function and higher overall satisfaction than those who performed CIC with or without onabotulinumtoxinA injection.

COMPLICATIONS

Short-term complications of AC are similar to those seen with other urinary diversions and include prolonged ileus (5.9%), wound infection (5%-6.4%), blood transfusion (11.7%), infections of ventriculoperitoneal shunt (0%-20%) and small bowel obstruction (3%-9.8%).[3, 8, 23]

Reoperation. The risk of reoperation in patients undergoing bladder augmentation is not negligible. A retrospective review of adults undergoing augmentation showed a reoperation rate of 40% after a median of 7.8 years of follow-up.[24] In that study a simultaneous incontinence procedure done at the time of enterocystoplasty was a predictor of future operation (HR 1.47). A multi-institutional review of contemporary data from the Neurogenic Bladder Research Group indicated a 90-day major complication rate of 12% in patients undergoing AC with CCC vs 15% in those undergoing augmentation only.[25] However, the rate of follow-up surgery was 42% in patients with CCC vs 18% in those with augmentation only. In our institutional experience 44.1% of patients had long-term complications with 17.6% requiring reoperation.[8]

Stomal stenosis. Approximately 75% of patients undergoing AC will undergo concomitant CCC to facilitate catheterization.[26] Rates of stomal complications are dependent on surgical technique, surgeon experience, location of stoma and body mass index. Husmann compared stomal complications at 10-year follow-up in 3 groups of pediatric patients undergoing either appendicovesicostomy, cecal bladder augmentation with a reinforced ileal-cecal valve or Monti-Yang tube.[26] Long-term stomal stenosis rates were similar between the groups and stomal revision rate was similar to our experience (11.8% in adults).[8]

Bladder perforation. Spontaneous or traumatic bladder perforation is an uncommon but serious complication that may occur after bladder augmentation, with mortality rates as high as 25%.[27,28] Incidence varies from 2% to 13% depending on the length of follow-up and sample size.[29–32] **Factors associated with perforation include choice of bowel segment used, ischemic injury to augmented segment, high bladder pressure or overdistention of bladder, catheter trauma, chronic infection and prior bladder neck closure.**[29–33]

In the largest retrospective study to date Metcalfe et al found an 8.6% rate of perforation in 500 augmented bladders over 25 years.[28] In that series increased risk of perforation was observed with use of sigmoid colon and bladder neck surgery. Husmann reported a significant relationship between bladder perforation and substance abuse as well as non-compliance with intermittent catheterization.[32] Intellectual disability was found in 16% of this population. The authors advocate for routine alcohol abuse screening as rates are similar to the general population (~12%). Additionally patients must repeatedly demonstrate the knowledge and ability to maintain proper bladder hygiene.

Diagnosis of bladder perforation is often delayed in patients with decreased sensation and may present with fever, tachycardia, vague abdominal pain, decreased urine output or inability to catheterize. A high index of suspicion is needed to intervene early and prevent further morbidity. Urgent decompression with maximal drainage is advocated in addition to early initiation of broad-spectrum intravenous antibiotics. For patients with an open bladder neck the placement of a large caliber urethral Foley catheter is recommended in addition to channel catheterization. **Imaging with computerized tomographic cystography is widely accepted as the gold standard, although if unavailable a static cystogram may demonstrate extravasation and allow diagnosis.** Inability to catheterize through the channel may be due to the creation of a false passage or kinking of the channel due to bladder overdistention. We recommend decompression either with urethral catheter or with bedside ultrasound guided aspiration.

Perforation usually occurs at the anastomosis of the bowel and bladder segments and often requires exploratory laparotomy with repair. Patients who are clinically stable with minimal urinary extravasation and/or a loculated fluid collection may be managed safely by percutaneous drain placement, intravenous antibiotics and maximal urinary drainage with the caveat that they must be monitored closely for clinical decompensation.[34]

Bladder stones. Presence of bladder stones is the most common complication following AC, affecting as many as 50% of patients with a recurrence rate as high as 50% within 5 years.[32, 35] Bladder stones occur in approximately 2% of patients who void via urethra but occur 5 times more frequently in patients with AC who require CIC, and up to 10 times more frequently in patients who catheterize through a channel.[3, 36] Cystolitholapaxy is the most common reoperation in patients with a history of augmentation, with rates ranging from 3.3% to 39%.[3, 24, 37] However, recurrence seems to be similar regardless of approach to stone removal (open or endoscopic).[38] Concomitant CCC is a significant predictor of future reoperation for stones (HR 2.92) vs use of catheterization per urethra (fig. 3).[24]

Bladder stone formation results from urinary stasis, increased mucus production that serves as a nidus for colonization and infection (ie struvite stones), presence of foreign bodies such as mesh or staples and underlying metabolic abnormalities of bowel absorption.[32, 39] Several studies have implemented interventions to mediate this risk. **In 1 study daily high volume bladder irrigations (≥240 cc) were associated with both a significant reduction in recurrent bladder calculi and a decrease in symptomatic UTIs**.[32] Using this management protocol, stone formation for all augmented patients with a continent channel decreased from a rate of 15% per decade of follow-up to slightly less than 5%. Additionally this study indicated that neither

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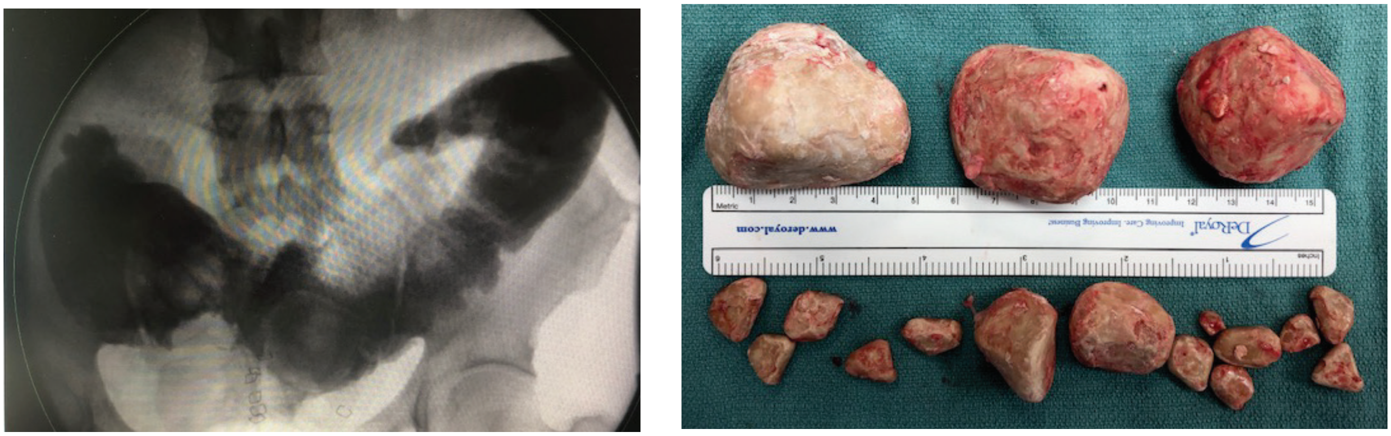

Figure 3. Patient with history of bladder exstrophy and augmentation cystoplasty with CCC who underwent open cystolithotomy for bladder stones.

the addition of mucolytic agents such as urea or acetylcysteine nor oral citrate supplementation to address hypocitraturia impacted stone recurrence rates. Stone-free rates remained similar at 63%-68% at 5 years regardless of added intervention as long as patients were compliant with daily high volume irrigation. Treatment of bladder stones may be approached with endoscopic cystolitholapaxy, percutaneous cystolitholapaxy or open cystolithotomy.

Renal calculi. Nephrolithiasis will develop in approximately 15% of patients, with a median time to stone development of 16 years.[32] Renal stones in neurogenic cases, which in the past were primarily struvite or carbon apatite, are increasingly observed to have primarily metabolic components.[40] Metabolic stone disease is common with an incidence of 23%-52%, with the most common abnormalities being chronic metabolic acidosis, hypocitraturia, elevated urine pH, hyperuricosuria, hyperoxaluria and low urine volume.[35,38] Metabolic evaluation with serum laboratory tests and 24-hour urine is recommended in all stone forming patients and can be helpful in preventing recurrence.

Gastrointestinal effects. Appropriate preoperative selection is key to avoiding gastrointestinal disturbances following surgery. Patients with inflammatory bowel disease, a history of fecal incontinence or chronic loose stool and those with short gut should be cautioned regarding the increased risk of postoperative issues. Resection of the terminal ileum may lead to fat and bile acid malabsorption, steatorrhea and chronic diarrhea. Decreased transit time may result in fecal incontinence and exacerbate malabsorption.[41,42] Removal of the IC valve, as seen in ileocecocystoplasty, may increase the risk of diarrhea, especially in patients with neurogenic bowel, who rely on constipation for fecal continence. However, even with removal of the IC valve the overall rate of loose stool is <3% in appropriately selected patients.[26] Fecal incontinence and/or diarrhea is usually correctable with 4-8 gm cholestyramine twice daily. Gastrointestinal motility inhibitors such as loperamide may also provide symptomatic relief.[43] Of note, over time small bowel obstruction occurs in approximately 5%-10% of patients, with up to half requiring operative intervention.[26,33,44]

Bacteriuria and urinary tract infections. Chronic bacteriuria in patients with bladder augmentation, which ranges from 45% to 85%,[26,32] has not been observed to contribute to renal deterioration. **It is therefore recommended not to treat positive urine cultures if patients are asymptomatic**. Symptomatic UTIs occur in 4%-43% of patients and are defined as a positive urine culture in the presence of fever, flank or lower abdominal pain, increase in spasticity or worsened urinary incontinence and/or foul smelling urine lasting more than 72 hours.[3,8,24] These patients should be treated with antibiotic therapy. Symptomatic infections are thought to be the result of urinary stasis, high residual urine volumes and increased mucus production. One study indicated that daily bladder irrigations ≥240 cc combined with catheterization at least every 6 hours were associated with a significant reduction in symptomatic UTIs.[32] Additionally gentamicin irrigation has shown efficacy in reducing the rate of symptomatic UTIs and courses of oral antibiotic treatment.[45]

Malignancy. The overall risk of bladder malignancy in patients who have undergone AC is low (1.2% to 4.6%).[46–48] The most common malignancy is adenocarcinoma, followed by urothelial carcinoma, predominantly occurring at the anastomosis of bowel and bladder.[46, 48] The mechanism of this increased risk is thought to be chronic inflammation and bacteriuria and conversion of urinary nitrates to nitrites by colonic bacteria to form N-nitrosamines, which are implicated in the formation of adenocarcinoma.[49]

The risk of bladder cancer, including urothelial cell carcinoma, is higher in patients with congenital bladder anomalies compared to the general population. However, it is unclear if enterocystoplasty is an independent risk factor as the majority of tumors are associated with chronic immunosuppression, prolonged tobacco exposure or inherent risk of malignancy such as in bladder exstrophy.[46,48,50,51] More recently, gastrocystoplasty has been associated with an increased incidence of both adenocarcinoma and urothelial cell carcinoma, ranging from 2.8% to 10.3%.[52, 53]

Given the long latency period and low overall risk, the timing and frequency of surveillance for bladder tumors are controversial for asymptomatic patients. **In patients with hematuria, unexplained urinary tract infections, new pain or new imaging findings it is imperative to rule out malignancy via cystoscopy.** Additionally consideration should be given to screening patients with gastrocystoplasty given their increased risk.

Vitamin B12 deficiency. **The terminal ileum is responsible for vitamin B12 absorption, and therefore removal may result in B12 deficiency and megaloblastic anemia.** The reported incidence of B12 deficiency in this population is approximately 38%.[54] Symptoms include megaloblastic anemia, which occurs early, and potentially irreversible demyelinating peripheral neuropathy, which occurs later. Stores of B12 in the bone marrow and liver typically last 3 to 5 years. **Therefore, it is recommended to check serum B12 levels annually 3-5 years after AC.**[55]

Therapies include monthly intramuscular parenteral injections of 1000 mcg vitamin B12 or daily sublingual vitamin B12 supplementation, both of which may be more effective than oral B12 in patients with altered absorption.[56] Some protocols advocate initiating oral B12 therapy (250 mcg daily) and rechecking serum B12 levels at 6 months.[54] If they remain low or if there is difficulty with compliance, parenteral or sublingual vitamin B12 supplementation can be used instead.

Metabolic derangements. The most common metabolic derangement, given the frequent use of ileum and colon, is hyperchloremic metabolic acidosis, which arises from increased absorption through the incorporated enteric segment. The bowel mucosal epithelium absorbs ammonium chloride and secretes bicarbonate. The extent to which this occurs depends on both the amount of bowel in contact and urine dwell time.[57] Hyperchloremic metabolic acidosis occurs in 5% of patients in the first decade following augmentation and increases to 15% by the third decade.[26] Treatment consists of supplementation with either potassium citrate or sodium bicarbonate when bicarbonate level falls below 21 mEq/ml. Calcium and vitamin D supplementation may be added to help prevent bone demineralization that may occur secondary to chronic acidosis.

Notably patients with glomerular filtration rate <45 ml per minute per body surface area are unable to compensate for the increased acid load that occurs with augmentation and are at further risk for severe metabolic acidosis. There is a theoretical risk of osteoporosis secondary to bone demineralization that takes place in the setting of chronic metabolic acidosis.

Colocystoplasty may be associated with hypokalemia due to potassium secretion by the colonic segment. Gastrocystoplasty typically results in a hypochloremic hyponatremic alkalosis.[3]

CONSIDERATIONS DURING PREGNANCY

In general, pregnancy and delivery are considered safe for women with a history of AC. The major concerns around childbearing include protection of the upper tracts, protection of the pedicle that supplies the reconstruction and an increased risk of ascending urinary tract infections. Patients with normal renal function at baseline do not have a significant risk of renal deterioration during pregnancy. However, those with preexisting renal insufficiency are at risk for additional deterioration during pregnancy.[58] Even patients with good baseline function may be at risk for obstruction requiring either stent placement or nephrostomy tube.[59] Frequent surveillance with renal ultrasound may be necessary during weeks 20-28 of gestation given the increased risk of obstruction during this time.

Successful childbirth with spontaneous vaginal delivery has been reported, and close collaboration with obstetricians with expertise in maternal-fetal medicine is advocated. The mesenteric pedicle is usually found overlying the uterus, and vascular compromise due to uterine growth has not been reported.[58] However, it is important that a urologist who is familiar with AC be involved in surgical intervention should cesarean section be necessary.

While asymptomatic bacteriuria is typically treated during pregnancy, there is no consensus on antibiotic treatment protocols in women with an augment that is mostly colonized.[58] The risk of pyelonephritis ranges widely (5%-60%). However, when it occurs, there is a risk of preterm labor, fetal loss and infant small for gestational age. Given these concerns, some advocate for daily prophylactic antibiotics in patients with augmentation, while others reserve antibiotic administration for high risk patients with renal compromise, recurrent symptomatic infections or hydronephrosis.[58,59]

Finally, catheterization of continent stomas may become more difficult with uterine distention. Use of a Coudé catheter may assist in traversing the channel. If this technique fails, an indwelling catheter may be required during pregnancy.[59] Fortunately most issues including difficulty catheterizing, incontinence, stomal prolapse and renal insufficiency resolve following pregnancy.

FOLLOW-UP OF PATIENTS WITH BLADDER AUGMENTATION

While there is no formal urological consensus on how to follow patients with bladder augmentation, recommendations are extrapolated from existing guidelines on the management of neurogenic bladder.[1,60–62] Annual visits are recommended for assessment of symptoms and physical examination, with particular attention to the stoma to evaluate for patency.[60] Serum metabolic panel is recommended at least annually. Vitamin B12 should be checked 3-5 years following augmentation if terminal ileum is used. If the patient remains stable, longer intervals may eventually suffice.

There is no consensus on the appropriate frequency of urodynamics following AC. Consideration should be given to performing urodynamics with fluoroscopy following any clinical change, such as worsening renal function, recurrent asymptomatic UTI or new incontinence, in order to evaluate the augment, presence of VUR, bowel peristalsis and bladder neck. Due to the risk of bladder stones and the importance of monitoring the upper tracts for deterioration, annual ultrasound is recommended with consideration of kidney, ureter, bladder plain film in patients with stone disease.[38] In high risk cases this imaging can be done as frequently as twice a year.[1]

If rising detrusor pressure/decreasing compliance or upper tract deterioration is noted during AC follow-up, further treatment may need to be considered. Traditionally this would be an additional augmentation. With the advent of onabotulinumtoxinA endoscopic approaches can be considered prior to repeat augmentation. Kaviani et al demonstrated the feasibility of injection of this agent into an augmented bladder, with the majority of injections directed to the native detrusor.[63] Compliance and capacity outcomes were mixed. If injection is attempted, enterocystoplasty cases should be followed closely afterward to ensure hydronephrosis and/or urodynamic parameters improve, and to allow additional intervention if they do not.

ADVANCES IN BLADDER AUGMENTATION AND REGENERATIVE MEDICINE

Minimally invasive approaches. Laparoscopic and robotic surgery are increasingly used in all aspects of urology, including bladder augmentation. Several series have demonstrated the feasibility of this approach.[64–67] Operative times are significantly longer and complication rates range from 40% to 60%.[64–66] Further work is needed to better understand the role and utility of such approaches.

ERAS protocols. Enhanced recovery after surgery protocols are increasingly used in urological procedures involving bowel resection and diversion. These protocols focus primarily on proactive approaches to pain and bowel management. Pain management avoids opioids and relies instead on regional anesthesia techniques and incorporation of scheduled alternatives.[68] Bowel management varies and typically does not involve preoperative bowel preparation, but can include 1) perioperative administration of alvimopan, 2) preoperative carbohydrate rich liquid nutrition, 3) early advancement of diet, 4) pharmacological prophylaxis of nausea/vomiting and 5) early mobilization.[69, 70] Pharmacological venous thromboembolism prophylaxis is often used as well. In the oncologic and reconstructive literature such protocols are now widely used and have been observed to decrease length of stay and postoperative complications.[68]

Alternatives to bowel for augmentation. The use of intestinal segments in AC is associated with significant morbidity, including but not limited to prolonged postoperative recovery, potential bowel complications, chronic metabolic disturbances, mucus formation and malignancy secondary to metaplasia. Therefore, approaches in regenerative medicine have been investigated to find an alternative material for augmentation.

A functioning bladder repetitively expands with low pressure and compliance to hold appropriate bladder volumes, and contracts to empty.[71, 72] The bladder must also maintain a watertight, non-absorbing surface to hold urine.[72] Augmented bladders must also remain effective for many years given the growing life expectancy of this patient population. These characteristics make it difficult to find an effective biomaterial for bladder augmentation.

An engineered bladder typically relies on several elements. A scaffold provides shape and initial mechanical strength. Biologic scaffolds include collagen and decellularized tissue matrixes such as small intestine and bladder submucosa, which have been touted for their biocompatibility and superior neovascularization.[71] Unfortunately the composition can vary greatly depending on the harvest source and in vitro development technique. More consistent and predictable, synthetic scaffolds include naturally derived polymers and silk based biomaterials. However, the long-term incorporation and durability of such scaffolds have been questioned. Recently composite scaffolds have been used in an attempt to combine the strengths of biologic and synthetic scaffolds.[72]

Scaffolds may be seeded with a variety of cells to stimulate in vivo regeneration, to promote vascularization and to supplement growth factors for vascularization.[72] While autologous homologous cells, ie from the patient's own bladder, would prove the least antigenic, using cells from diseased bladder is a cause for concern.[71] Therefore, a variety of other sources have been explored. Thus far, mesenchymal stromal cells such as bladder derived smooth muscle cells, adipose derived stem cells, bone marrow stem cells, endometrial cells and urine derived stem cells as well as induced pluripotent stem cells have been investigated. It is important to note that non-bladder derived stem cells may react unpredictably when in prolonged contact with urine in vivo.

Five human trials have been conducted, with 2 in the neurogenic bladder population, which have produced mixed results. Atala et al used autologous bladder urothelial and muscle cells seeded on a composite collagen-polygycolic acid scaffold in patients 4-19 years old with myelomeningocele.[73] Initially patients experienced larger bladder capacities and longer dry periods, and urodynamics revealed increased compliance and reduced end filling pressures. Interestingly patients with an omental wrap over the augment seemed to fare better. However, significant fibrosis was noted in the artificial bladder wall on follow-up. Joseph et al used a similar autologous cell seeded composite scaffold in a comparable patient population and found no improvement in capacity or compliance.[74] In addition, several severe complications were noted, including bladder rupture and bowel obstruction, and most patients eventually converted to a traditional enterocystoplasty. Since that time, further human studies have not been pursued.

The other 3 studies, which investigated bladder function of mixed etiologies, used unseeded biomatrixes.[71] On follow-up these series indicated low concentration of muscle fibers within the scaffold. Translation to human studies has met with disappointing results. Further work is needed before regenerative medicine becomes a viable alternative to enterocystoplasty.

CONCLUSIONS

Augmentation cystoplasty is the gold standard for patients with end stage disease or at risk bladder secondary to poor compliance and capacity. If enteric segment is used, functional and urodynamic outcomes following surgery are improved and durable over time. However, despite reliable clinical outcomes and high satisfaction among patients, reoperation rates are high. Patients are at risk for complications, and annual monitoring is necessary to prevent morbidity and mortality. Emerging advancements in regenerative medicine present an exciting frontier in the area of augmentation.

DID YOU KNOW?

- Augmentation cystoplasty is the gold standard for patients with failed conservative management.
- Diagnosis of bladder perforation is often delayed in patients with decreased sensation. A high index of suspicion is needed to intervene early and prevent further morbidity.
- When perforation is suspected, imaging with computerized tomographic cystography is widely accepted as the gold standard.
- Daily high volume bladder irrigations (≥240 cc) are associated with a significant reduction in recurrent bladder calculi and a decrease in symptomatic UTIs.
- Treatment for positive urine cultures is not recommended if patients are asymptomatic.
- In patients with hematuria, unexplained urinary tract infections, new pain or new imaging findings it is imperative to rule out malignancy via cystoscopy.

Appendix 1. Augmentation cystoplasty indications and contraindications

INDICATIONS
• Infection (eg tuberculosis, schistosomiasis) • Inflammatory disorders (eg radiation cystitis, chemotherapy cystitis) • Prior to renal transplantation • Neurogenic bladder (eg stroke, spinal cord injury, congenital)
CONTRAINDICATIONS
• Intrinsic bowel disease • Congenital bowel anomalies • History of enteric radiation* • Insufficient functional bowel length • Poor manual dexterity • Glomerular filtration rate <45 ml/min/body surface area*

*Relative contraindication.

Appendix 2. Advantages and disadvantages of enteric segments

Bowel Segment	Advantages	Disadvantages
Ileocystoplasty	Decreased risk of metabolic derangements	May have short mesentery
Sigmoid colocystoplasty	Large capacity Easily accessible mesentery	Increased mucus production Colonic contractions result in higher pressures
Ileocecocystoplasty	IC valve may be used as a continence mechanism	Potential for diarrhea/increased risk of malabsorption
Gastrocystoplasty	Less mucus production Reduced infection risk Reduced risk of metabolic derangements	Risk of hematuria-dysuria syndrome Increased malignancy risk

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Study Questions Volume 39 Lesson 23

1. A 34-year-old man with a history of a spinal cord injury and ileocystoplasty with a continent catheterizable channel presents with a 12-hour history of an inability to catheterize, fever to 101.5°F and abdominal distention. The next immediate step is
   a. bladder decompression with catheterization
   b. computerized tomographic cystogram
   c. oral antibiotics
   d. emergent exploration

2. The risk of perforation of an augmentation cystoplasty increases when there is
   a. more than 10 years elapsed since time of augmentation
   b. ileum used as the enteric segment
   c. a prior bladder neck closure
   d. a catheterizable stoma

3. A 40-year-old woman with a continent catheterizable stoma and ileocystoplasty experiences bladder stones 3 years after her surgery. Her stones are removed with endoscopic cystolitholapaxy and are noted to be magnesium triphosphate. The next step to prevent further stones is
   a. 24-hour urine measurement of calcium, uric acid, magnesium and citrate
   b. potassium citrate supplementation
   c. regular bladder irrigation
   d. prophylactic antibiotics

4. Surveillance following augmentation cystoplasty, regardless of the bowel segment used, should routinely include yearly
   a. serum B12
   b. cystoscopy
   c. videourodynamics
   d. upper tract imaging

5. Cystoscopy is indicated following augmentation cystoplasty
   a. yearly in all patients as part of routine follow-up
   b. yearly in patients with an ileocystoplasty
   c. yearly in patients with a smoking history
   d. with new onset hematuria

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