

## Treatment and Prevention of Urinary Tract Infections in Spinal Cord Injured Patients\*

*Learning Objective:* At the conclusion of this continuing medical education activity, the participant will be able to review how to diagnose and treat UTI in a SCI patient, identify risk factors for UTI in a SCI patient and outline UTI prophylaxis strategies for SCI patients.

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## INTRODUCTION

Urinary tract infections are a significant problem for spinal cord injured patients. Untreated UTIs in a SCI patient can lead to significant morbidity such as pyelonephritis or sepsis. However, SCI patients can also be subjected to over screening and treatment for suspected UTIs, which can cause antibiotic resistance and financial burden. The purpose of this AUA Update is to review how to diagnose and treat UTI in a SCI patient, identify risk factors for UTI in a SCI patient and outline UTI prophylaxis strategies for SCI patients.

## UROLOGISTS AS PART OF THE SCI CARE TEAM

Spinal cord injury is a prevalent condition. In North America a spinal cord injury occurs in about 25-59 per million people.<sup>1</sup> **Extrapolated, these numbers translate to approximately 12,000-17,000 new spinal cord injuries per year.** A recent publication suggests that while the overall incidence of SCI has been stable from 1993–2014, the incidence rose dramatically in men 65-74 years old within this time frame from 84 to 131 cases per million people because of more traumatic falls in these age groups.<sup>2</sup>

After a spinal cord injury, urinary frequency/urgency and urinary incontinence are common and significantly impact many aspects of a person's quality of life.<sup>3</sup> Urinary symptoms after SCI can also signify low bladder compliance, urinary calculi, bowel complications and urinary tract infections. Care teams frequently rely on the urologist to make the determination if urinary symptoms represent a safety or quality of life issue. However, many SCI patients do not have good access to urological care. In a 2015 National Institute of Diabetes and Digestive and Kidney Diseases sponsored study on **Urologic Diseases in America**, Cameron et al reported that only 36% of SCI patients from a 5% Medicare sample saw a urologist within the studied 2-year interval.<sup>4</sup> **Urologists are often underutilized members of the SCI patient care team which can impact how urinary tract infections are treated.**

## INCIDENCE OF UTI IN A SCI POPULATION

A retrospective data review of all traumatic spinal cord injury patients in Ontario, Canada between 2002 and 2013 showed that 40% of SCI patients in their cohort experienced a "serious UTI" requiring hospitalization or emergency room visit at some point during follow-up.<sup>5</sup> SCI patients may be particularly vulnerable to UTI within the first year of injury, with one study noting that urinary tract infection was the most commonly reported complication (62% of 169 adults), followed by autonomic dysreflexia (43%) and pressure ulcers (41%).<sup>6</sup> A high UTI incidence among SCI patients is also seen in insurance claims data.<sup>7</sup> SCI patients also self-report UTIs in cross-sectional studies. The Neurogenic Bladder Research Group prospectively followed a cohort of SCI patients performing

intermittent catheterization for a year and noted that 28% self-reported having >4 UTIs per year and 10% had been hospitalized because of a UTI within the last 12 months of the study.<sup>8</sup>

## DIAGNOSING A UTI IN A SCI PATIENT

*Definitions.* There are no universally accepted definitions for urinary tract infections in SCI populations, which makes it unclear if SCI patients are over or under treated for the condition. This is highlighted in a review article on UTI after onabotulinum toxin injection showing that 27 publications used 10 different definitions to identify a UTI.<sup>9</sup> Consequently, practitioners should be aware of generalities and specifics that can be used in diagnosing a UTI in SCI patients.

A urinary tract infection in a patient with neurogenic bladder can be defined as new onset signs and symptoms accompanied by urinalysis showing leukocytosis, bacteriuria and a positive urine culture. However, **urine culture should be routinely performed as part of the evaluation in SCI patients, even if positive findings are found on urinalysis, so that bacteria can be correctly identified and the proper antibiotic regimen selected.** Using definitions from several societies, the summary definition of bacterial cystitis is shown in Appendix 1.<sup>10-12</sup>

Practitioners should also be familiar with 2 additional specific diagnostic definitions when evaluating SCI patients for UTI, namely catheter acquired urinary tract infection and asymptomatic bacteriuria.

*Catheter acquired urinary tract infections.* Many SCI patients use indwelling urinary catheters or perform intermittent catheterization. Diagnosing a UTI in these patients can be challenging and the CAUTI definition continues to evolve. **When assessing for CAUTI, urine should be obtained from a new urinary catheter. Urine obtained from a collection bag, even if new, should be considered contaminated and culture data should be interpreted with skepticism.** Although there is no single best definition of CAUTI, this Update combines recommendations from several sources to present a summary definition (Appendix 1).<sup>13-17</sup>

*Asymptomatic bacteriuria.* The Infectious Diseases Society of America recently published recommendations regarding screening and treatment for patients with asymptomatic bacteriuria.<sup>18</sup> The society recommended that screening for asymptomatic bacteriuria should only be performed in pregnant women and individuals who are undergoing invasive urological procedures. **Treatment of asymptomatic bacteriuria was not recommended for people with indwelling catheters or spinal cord injury.** Consequently, it is important to always determine if symptoms are present when presented with a positive urine culture in SCI patients.

## COMMON UTI SYMPTOMS, SIGNS AND ORGANISMS

Diagnosing a UTI in SCI patients requires matching a positive culture to concomitant symptoms that are consistent with a UTI. In a neurologically intact population, symptoms and signs typically associated with a UTI include increased urinary frequency, urgency, new incontinence, change in bladder capac-

**ABBREVIATIONS:** AUA (American Urological Association), CAUTI (catheter acquired urinary tract infection), CIC (clean intermittent catheterization), DSD (detrusor sphincter dyssynergia), SCI (spinal cord injury), UTI (urinary tract infection)

ity, change in urine color or odor, and suprapubic pain. However, spinal cord injury patients frequently have an altered sensorium, baseline lower urinary tract symptoms and catheters to assist bladder emptying. Consequently, many SCI patients do not endorse these “typical” UTI symptoms. It is recommended that practitioners query the patients about other **symptoms that can be associated with UTI in SCI patients such as new onset weakness, significantly increased spasticity or dysreflexia, increased urinary incontinence, and confusion.**<sup>15, 19</sup> It is important to note that many SCI patients with severe bladder symptoms likewise have similarly severe bowel symptoms,<sup>20</sup> which can be misinterpreted as evidence of a UTI. However, practitioners should be aware that generalized symptoms are not strongly predictive of a culture-positive UTI in SCI patients. For example, one study examined how often SCI patients were correct in diagnosing their symptoms as a UTI and found that the positive predictive value of urinary symptoms for UTI was only 33%.<sup>21</sup>

The specific bacteria responsible for a SCI UTI may depend on the time from injury and setting where the culture was taken. Patients with a new spinal cord injury are at most risk for a hospital acquired urinary tract infection during initial hospitalization. Organisms associated with hospital based infections include *Escherichia coli*, *Klebsiella*, *Enterococcus* and *Enterobacter*.<sup>22</sup> Depending on a hospital’s multidrug resistant organism biome, SCI patients may be at greatest risk for multidrug resistant organism UTIs during this time frame, which can prolong the hospital stay. The bacteria in SCI UTIs treated in a community setting may differ from hospital acquired UTIs. In a Korean epidemiological study comparing SCI patient UTI organisms from hospital versus community setting, the proportion of Enterobacter from hospital-dwelling patient cultures was lower than that from community-dwelling patients (66.0 vs 85.5%,  $p < 0.001$ ) and the proportions of Pseudomonas, Acinetobacter and Enterococcus species were higher (8.7%, 6.0% and 12.0% vs 2.8%, 0.7% and 2.8%, respectively,  $p < 0.05$ ).<sup>23</sup> Given the frequent hospitalization risk of SCI patients, **it should be routine to inquire whether a SCI patient with symptoms and a positive urine culture has had a recent hospitalization.** This information may better inform antibiotic selection.

SCI patients with proteus positive urine cultures either in hospitals or the community may be at increased risk for morbidity. Hung et al followed 501 SCI patients and identified 71 with positive proteus urine cultures.<sup>24</sup> Proteus was significantly associated with increased risk for hospitalization, decubitus ulcers and urinary stones in this cohort. As expected, positive proteus cultures were also associated with indwelling urinary catheters.

## RISK FACTORS FOR UTI IN SCI PATIENTS

SCI UTIs may be caused by an underlying pathophysiology that may predispose the patient to recurrent UTIs. Several models for categorizing UTI risk factors in SCI patients have been presented. Domains of these models have included bladder storage, impaired washout, catheterization, functioning level of person and intrinsic defense mechanisms.<sup>25-27</sup> This Update discusses selected risk factors from these domains.

**Bladder overdistension.** As early as 1972, Lapedes et al noted that overdistension of the bladder decreased blood flow to the bladder.<sup>28</sup> They postulated that the resulting ischemia left the bladder susceptible to infection from colonizing bacteria,

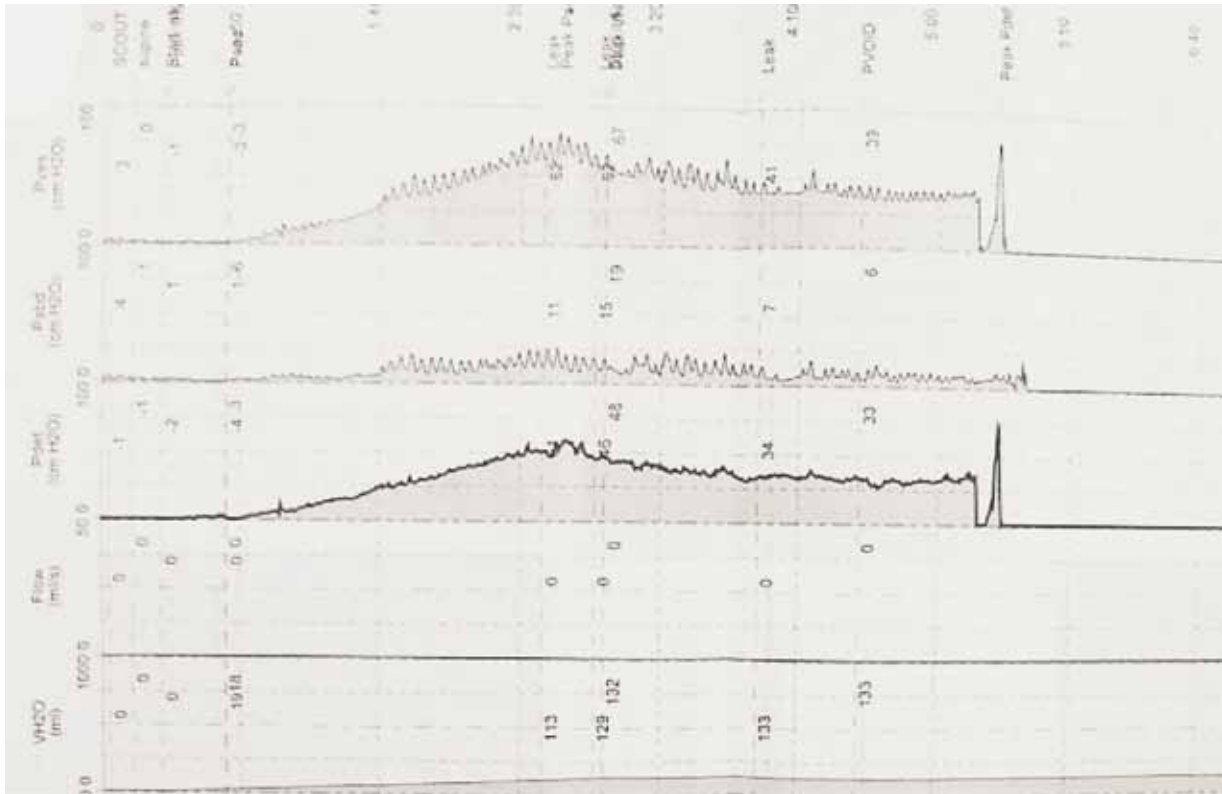
particularly from the gastrointestinal tract. Other investigators have also endorsed this hypothesis.<sup>26, 27</sup> Bakke et al followed 170 spinal cord injury patients from 1988-1995 and found those with the highest mean catheterizable volumes (>400 ml) during this time had reported the most urinary tract infections.<sup>29</sup> Krebs et al also reported a low incidence of UTI among SCI patients with minimal residual volume after CIC.<sup>30</sup> Consequently, it is recommended that SCI patients with recurrent UTIs and high standing volumes catheterize more frequently.

**Low bladder compliance.** Low bladder compliance in spinal cord injury patients, defined as change in infused bladder volume/change in detrusor pressure during urodynamic testing, is a known risk factor for urinary tract infections and pyelonephritis.<sup>27, 31</sup> It is thought that detrusor high pressures can precipitate UTIs/pyelonephritis by causing vesicoureteral reflux, urine stasis in upper tracts, or ischemia in the detrusor muscle. Although threshold values have not been validated across populations, **it is commonly accepted that compliance calculations of <10-20 cc/cm H<sub>2</sub>O represent low compliance.**<sup>27, 32, 33</sup> It has been reported that up to 30% of SCI patients have had low bladder compliance, including complete and incomplete injury categories.<sup>34</sup> Low bladder compliance can be treated with anticholinergic or beta-3 agonist medications, onabotulinum toxin injections and bladder augmentation for appropriate patients. Figure 1 shows a urodynamic tracing of low bladder compliance in a SCI patient. Note that given the potential risk of UTI, the American Urological Association recommends antibiotic prophylaxis prior to urodynamic evaluations of spinal cord injury patients.<sup>35</sup>

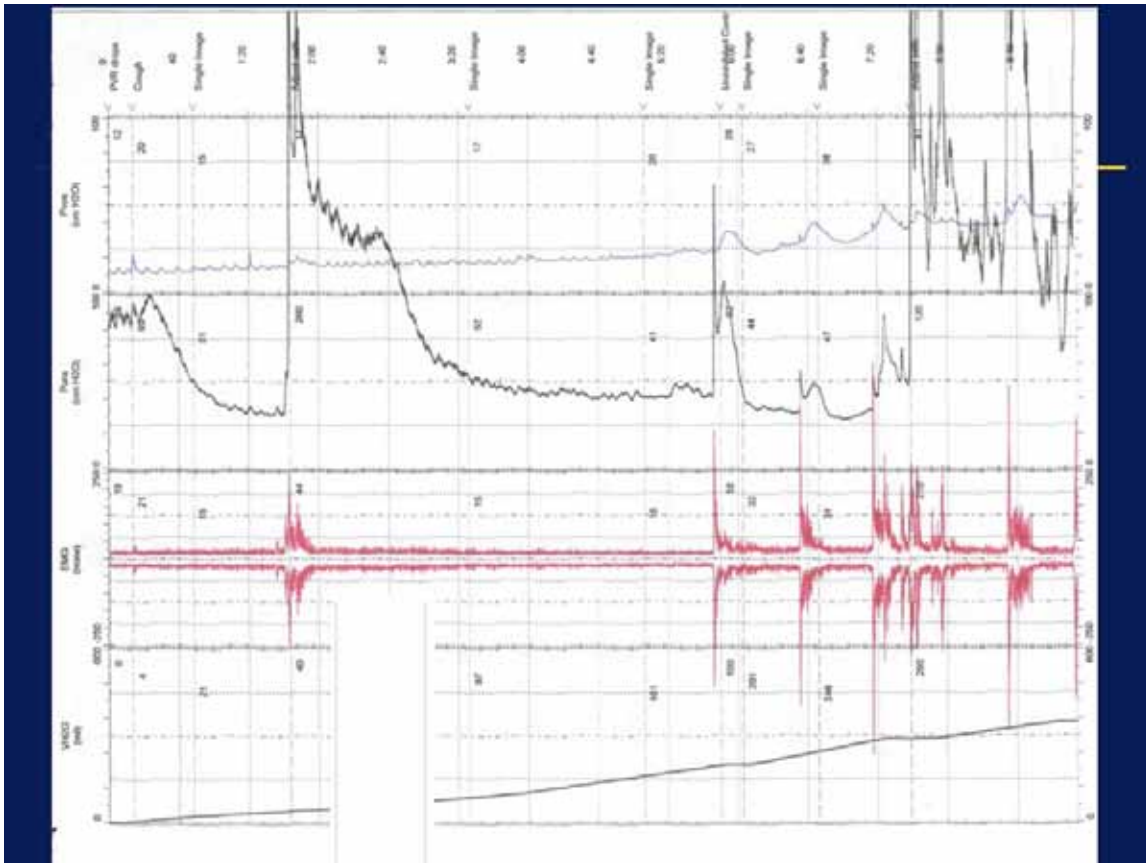
**Detrusor sphincter dyssynergia.** DSD represents mechanical obstruction from the detrusor contracting against a non-relaxing urethral sphincter.<sup>36</sup> Although data are limited, retrospective data suggest that this physiology is a risk factor for upper tract changes and UTIs in SCI patients,<sup>36, 37</sup> likely by causing low bladder compliance changes from the high grade bladder outlet obstruction. Treatment for DSD includes changing from reflexive voiding to intermittent catheterization, anticholinergic or beta-3 agonist medications, and onabotulinum toxin to detrusor and/or sphincter. Figure 2 shows a urodynamic tracing demonstrating DSD (electromyography and urethral pressure changes) in a SCI patient with concomitant bladder compliance changes.

**Urinary calculi.** Spinal cord injury patients are at risk for urinary calculi because of a combination of urine stasis and reabsorptive hypercalciuria from immobility. Stones are common in the SCI population. In 2 separate longitudinal institutional cohorts 49% and 17% of SCI patients experienced a bladder or renal stone, respectively.<sup>38, 39</sup> It can be challenging to determine if urinary calculi are contributing to positive urinary cultures in SCI patients. **Most practitioners will treat bladder stones when identified to decrease the risk of continued irritative urinary symptoms and positive urine cultures. American Urological Association renal stone treatment guidelines recommend surgical treatment of the stone in the setting of staghorn calculi unless comorbid conditions preclude obstruction, infection and symptoms.**<sup>40</sup>

**Urinary catheters.** CIC is commonly used among SCI patients, both immediately after injury and in subsequent years.<sup>3</sup> However, the technique is associated with an increased risk of UTI. Kennelly et al reported that UTI is the most common complication associated with CIC and cite that UTI incidence rates were



**Figure 1.** Low bladder compliance in SCI patient (133 cc infused/33 cm H<sub>2</sub>O detrusor pressure=4 cc/cm H<sub>2</sub>O).



**Figure 2.** Urodynamic tracing of DSD. Note spike in urethral pressure (Pura) and electromyography during evidence of detrusor overactivity write out on vesical pressure (Pves) at volumes of 40, 190 and 246 cc. Vesical pressure shows rise of pressure after 200 cc, indicating loss of compliance.

between 2 and 10 per year during the acute rehabilitation phase and ranged from 0.8–3.5 per year after leaving rehabilitation.<sup>27</sup> UTIs have also been cited as a major reason that SCI patients abandon CIC for bladder management.<sup>41</sup> **Contradicting a past Cochrane review that has since been withdrawn,<sup>42</sup> recent studies suggest that patients performing CIC using single use hydrophilic catheters may have fewer UTIs than those using multiuse PVC catheters.**<sup>43,44</sup> Hygiene and good catheterization technique likely also play significant roles in preventing UTIs. However, the number of times per day that CIC is performed has not been conclusively shown to impact the risk of UTI in SCI patients.<sup>45</sup>

Indwelling urinary catheters have long been thought to be associated with increased risk of UTI in SCI patients. Hennessey et al prospectively followed 143 newly injured SCI patients and found that those with an indwelling urethral catheter after injury had the highest incidence of UTI (8.7/1000 inpatient days) compared to suprapubic tube (3.8/1000 inpatient days,  $p=0.007$ ).<sup>46</sup> After the acute injury phase, SCI patients who use indwelling urethral catheter or suprapubic tube have also been shown to have a higher incidence of multidrug resistant organisms on urine culture compared to other management techniques.<sup>47</sup>

*Neurogenic bowel.* Neurogenic bowel in SCI patients involves changes in colon motility and anorectal sphincter function. Spinal cord injuries above L1–L2 are associated with increased bowel motility and high anorectal sphincter tone while injuries below L2 are more likely to cause an areflexic colon and low sphincter tone.<sup>48</sup> There are data to suggest that bowel programs that reduce stool transit times and improve fecal continence can minimize urinary tract infections. Transanal irrigation programs, in particular, have been projected to potentially reduce UTI incidence by a third in SCI patients with underlying constipation.<sup>49,50</sup>

*Immunosuppression.* It is thought that an acute SCI can cause a secondary immunosuppression. After an injury, increased hypothalamus-pituitary-adrenal signaling leads to overactive noradrenergic and glucocorticoid production.<sup>51</sup> Research has suggested that these high levels of stress hormones may cause lymphocyte apoptosis, particularly in SCI patients with high level injuries.<sup>52</sup> This immunosuppression may help explain why SCI patients are particularly vulnerable to infections, such as UTI and pneumonia, within the first year of injury (Appendix 2).

## TREATMENT OF SYMPTOMATIC UTI

*Antibiotic therapy.* Clinicians should only treat symptomatic, culture proven urinary tract infections in SCI patients. Asymptomatic bacteriuria should not be treated unless the patient is undergoing an invasive urological intervention. **Although there is no consensus agreement, it has been recommended that practitioners choose a 5 to 7-day treatment plan for SCI patients with new UTIs without fevers, 7 to 10-day treatment plan for recurrent UTIs without fevers and 14 days for SCI patients with fevers.**<sup>53-56</sup> Antibiotic courses greater than 15 days do not seem to add further benefit, even with febrile UTIs.<sup>57</sup> However, clinical judgment should be used and the antibiotic duration extended if soft tissue abscess, osteomyelitis or visceral fistula are involved. A narrower spectrum antibiotic, such as nitrofurantoin, fosfomycin or trimethoprim, should be the first choice if local resistance patterns permit. Fluoroquinolones

should be reserved for UTIs in patients with established prior resistance or rapidly progressing infections.<sup>54</sup> Monotherapy has been shown to be equally efficacious as dual antibiotic therapy.<sup>57</sup> Intravenous or intramuscular antibiotics are appropriate for highly resistant organisms and for patients at risk for sepsis. For the SCI patients requiring immediate intravenous antibiotic before culture data are available, a broad spectrum parenteral beta lactam is usually recommended for 72 hours or until specific organisms and resistance are identified on cultures.<sup>56</sup> Antibiotics can then be adjusted appropriately.

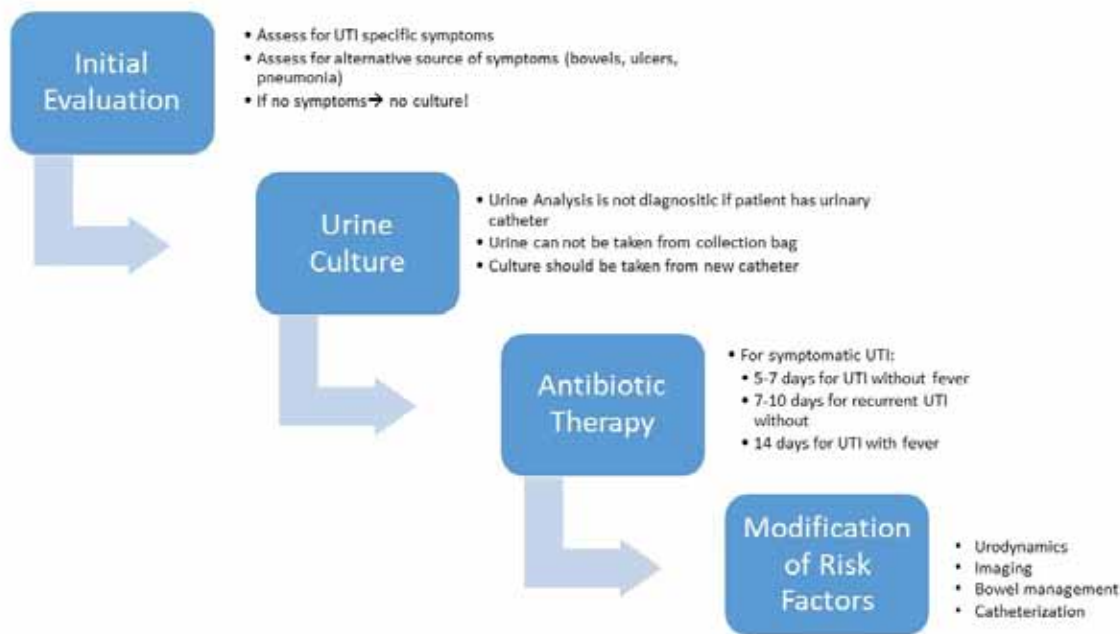
SCI patients with CAUTI may benefit from first changing the catheter before obtaining a urine culture and initiating treatment. In one study examining the microbiome of SCI patients with symptomatic UTIs, more than 2 organisms were found in 14% of patients performing intermittent catheterization, 67% of patients with suprapubic catheters and 71% of patients with indwelling urethral catheters.<sup>58</sup> A new catheter may also help reduce antibiotic treatment times. Darouiche et al compared the efficacy of a 5-day antibiotic treatment in patients with a new catheter compared to 10-day treatment for patients with the same catheter and found no difference in response rates, although the sample size was limited.<sup>59</sup>

*Antibiotic alternatives.* Non-steroidal medications in particular have been suggested as alternative therapies for uncomplicated urinary tract infections. Several trials have been performed in the gynecologic literature, but the findings suggest that nonsteroidal anti-inflammatory drugs are inferior in reducing urinary tract infection symptoms and may increase the risk of pyelonephritis.<sup>60,61</sup> No other non-antibiotic compound has proven to be an effective treatment for a symptomatic UTI and their use cannot be recommended for SCI patients as alternative treatments (fig. 3).

## PREVENTION OF RECURRENT UTI

Recurrent UTIs have a significant impact on a spinal cord injured patient's safety and quality of life. Although there is no standard definition for recurrent UTI in the SCI population, it is generally thought that patients with >3 UTIs per year or >2 UTIs per 6 months meet the criteria. When developing a prevention strategy for these patients, it is important to first review the cultures and confirm that the patients indeed had positive urine cultures that were temporally associated with symptoms consistent with a UTI. If confirmed, the practitioner should next review the culture data to determine if the cultures are different organisms or the same recurrent organisms. A recurrent organism may reflect an incompletely treated UTI, urinary calculi or an abscess. Imaging such as computerized tomography urogram may be warranted for these patients.

*Antibiotic prophylaxis.* **Antibiotic prophylaxis is not recommended for SCI patients without urinary tract infections who perform intermittent catheterization or have a suprapubic tube.** Some SCI patients with recurrent UTIs may benefit from antibiotic prophylaxis but there is controversy regarding the effectiveness of these treatments. Some studies have shown efficacy. A matched pairs study matched 122 Veterans Administration spinal cord injury patients on >90 days of nitrofurantoin to 196 controls and found that the nitrofurantoin group had fewer UTIs.<sup>62</sup> Chew et al also found no evidence that nitrofurantoin promoted resistant organisms. Other groups have advocated for alternating a weekly oral alternating single antibiotic regimen as an alternative to a single drug prophylaxis strategy. Alter-



**Figure 3.** Assessment and treatment algorithm for SCI UTI.

nating fosfomycin and amoxicillin for gram-positive bacteria and alternating trimethoprim, fosfomycin, nitrofurantoin or cefixime for gram-negative organisms, Salomon et al showed a reduction of UTIs from 9.4 to 1.8 per patient per year.<sup>63</sup> However, prior to these studies a 15-trial meta-analysis in 2002 did not demonstrate a reduction in symptomatic UTIs among SCI patients on prophylaxis.<sup>64</sup> However, the analysis did note a reduction of asymptomatic bacteriuria. The meta-analysis was limited by varying definitions of urinary tract infection and mixed populations.

**Bladder washes with antibiotics have also been reported as alternatives to oral medications for UTI prophylaxis.** Cox et al published a prophylaxis protocol in which a cohort of patients, which included SCI, instilled a dose of 14.4 mg gentamicin/30 ml or 28.8 mg/60 ml into the bladder with the solution left indwelling until the next catheterization.<sup>65</sup> Patients on this regimen had fewer symptomatic UTIs (median 4 episodes vs 1,  $p < 0.004$ ). Abrams et al found a similar reduction in UTI incidence using a lower dose of intravesical gentamicin.<sup>66</sup> Neomycin-polymixin (1 to 4 ampules of GU irrigant diluted in 1 liter normal saline) was also shown to reduce the incidence of symptomatic UTIs by 58% and ER visits by 54% in a pediatric neurogenic bladder cohort.<sup>67</sup>

**Cranberry supplements.** Cranberry is a popular over the counter supplement that is used for prevention of urinary tract infections due to a compound in the berry that may inhibit bacterial adherence to the bladder wall. A few studies have investigated its use in the spinal cord injury population. Hess et al performed a randomized, double-blind crossover study with 47 SCI patients and found that during the period in which the subjects were taking cranberry, 7 UTIs were reported in 6 patients, compared with 21 UTIs in 16 subjects while not taking cranberry ( $p < 0.05$ ).<sup>68</sup> In contrast, a different 21-patient, randomized, placebo controlled blinded study did not note

any difference in UTI incidence between cranberry treatment and control arms.<sup>69</sup> Investigation of the efficacy of cranberry in reducing CAUTI in a non-neurogenic population did not show benefit in reducing UTIs. Although there is no strong directional evidence to inform usage in **spinal cord injury patients, a recent meta-analysis of 28 non-neurogenic cranberry supplements trials stated that cranberry appears to be protective in a general population and reduced the UTI incidence by more than 60%.**<sup>70</sup> Care should be taken when extrapolating these expectations to patients with complex urinary tract infections or indwelling catheters.

**Methenamine salts.** Methenamine salts are thought to prevent urinary tract infections through the production of a bacteriostatic compound, formaldehyde. It is unclear if the mechanism of action is directly bacteriostatic or if the compound acidifies the urine and thus changes the local environment in the bladder. There are several trials investigating the effectiveness of methenamine in preventing urinary tract infections. **A 2012 Cochrane review evaluated 13 studies and in a subgroup analysis concluded that methenamine was ineffective in preventing UTIs in patients with underlying renal abnormalities and/or neurogenic bladder.**<sup>71</sup> Despite little data that suggest strong benefit, methenamine salts continue to be used due to their low side effect profile and low probability of selecting for multidrug resistant organisms.

**Bacterial interference/immunomodulation therapy.** Many SCI patients have bacterial colonization in the bladder but do not experience symptomatic urinary tract infections. It is thought that benign bacterial colonization may be interfering with more pathogenic strains. This strategy of bacterial interference has been investigated as a potential option for UTI prophylaxis. Hull et al examined outcomes of 21 patients with neurogenic bladder purposely colonized through intravesical instillation with a specific strain of *E. coli* (83972) to prevent UTIs.<sup>72</sup> Only



61% of patients successfully achieved colonization and these patients maintained colonization over a mean of 12 months. While colonized, no patients experienced symptomatic UTIs. Other E. coli variants have also been studied by this investigative group but little has been published since these initial studies.

Oral immunomodulation therapy with biotechnologically produced antigens E. coli strains may also provide a new alternative treatment options for preventing recurrent UTIs in SCI patients. Krebs et al recently described an approximately 30% reduction in UTI incidence in 136 SCI patients who were taking lyophilized lysate of 18 E. coli strands.<sup>73</sup> This intervention is currently not approved in the U.S. but may provide an interesting modality in the future.

**Reconstructive surgery. It is important to note that some SCI patients may continue to have chronic urinary tract infections despite aggressive preventive measures due to refractory bladder physiology, physical challenges or lack of supplementary caregiver support. Urologists should discuss reconstructive urological options with these patients.** Some patients who cannot perform intermittent catheterization while in a wheelchair may benefit from a bladder augment and continent catheterizable channel. However, patients should be counseled that bladder augment surgery can be associated with bladder stones and chronic UTIs over long-term follow-up.<sup>74</sup> The author of this Update offers a retropubic Boari bladder flap continent channel for SCI patients with a >500 cc capacity bladder without overactivity and inability to catheterize per urethra as an alternative to a bowel based stoma.<sup>75</sup> Urinary diversion has also been successfully used as a treatment for refractory UTIs in other neurogenic bladder populations, such as multiple sclerosis.<sup>76</sup>

## CONCLUSIONS

Identifying, treating and preventing urinary tract infection present an ongoing challenge for patients with spinal cord injuries and the teams who provide care for them. Diagnosing a UTI requires both symptoms and a positive urine culture. Asymptomatic spinal cord injury patients should neither be screened for UTIs nor treated based on a positive urine culture. Many risk factors can contribute to the development of a UTI and practitioners should review all possible etiologies to reduce the risk of recurrent UTIs. There is no single best prophylaxis regimen to prevent recurrent UTIs and, as data are lacking, an informed discussion regarding risks and benefits should help shared decision making between patients and treating practitioners.

### DID YOU KNOW?

- Diagnosing a UTI in a spinal cord injury patient requires both a positive urine culture and symptoms consistent with a UTI for this population.
- Screening cultures should not be performed and asymptomatic bacteriuria should not be treated.
- Antibiotic treatment length of a UTI ranges from 5-14 days, depending on severity and catheter status.
- Risk factors for UTIs in SCI patients include as bladder overdistension, low bladder compliance, detrusor sphincter dyssynergia, urinary calculi and indwelling catheters.
- Prophylaxis against UTIs is challenging in the SCI population and, other than modifying risk factors, there are no universally accepted treatments.

## Appendix 1. Definitions

<b>Bacterial Cystitis Definition:</b>
• Symptoms consistent with UTI
• Pyuria >10 WBC/high powered field (×400 magnification) in resuspended sediment of centrifuged urine
• >102 colony forming units (cfu) if collected via catheterization
• >104 cfu if collected from midstream urine
• Any concentration of bacteria if collected via suprapubic aspirate
<b>CAUTI Definition (summarized):</b>
• Patient needs to display signs and symptoms consistent with UTI
• >103 cfu in patients using CIC, urethral catheter, suprapubic tube
• >103 cfu in patients with previous catheter removed within 48 hours
• Positive fungal cultures are not diagnostic of UTI in a hospitalized catheterized patient
• Pyuria or other urinalysis findings are not diagnostic of UTI in catheterized patient
• Patients with reconstructed urinary tracts (diversions, bladder augments) will likely have colonization at baseline which should be considered when interpreting cultures
<b>Asymptomatic Bacteriuria Definition:</b>
• 1 or more species of bacteria in urine >105 cfu
• No signs or symptoms of UTI
• Pyuria may be present on urinalysis

## Appendix 2. Potential risk factors for UTI in SCI patients and possible interventions

Risk Factor	Possible Intervention to Avoid Recurrent UTI
Bladder overdistension	<ul style="list-style-type: none"> <li>• Void or catheterize to keep volumes &lt; 400 cc</li> <li>• Avoid obstruction of indwelling catheter</li> </ul>
Low bladder compliance	<ul style="list-style-type: none"> <li>• Anticholinergic or beta-3 agonist medication</li> <li>• Onabotulinum toxin injections</li> <li>• Bladder augment/urinary diversion</li> </ul>
Detrusor sphincter dyssynergia	<ul style="list-style-type: none"> <li>• Reduce contractility of bladder with anticholinergic medications or onabotulinum toxin</li> <li>• Avoid spontaneous or reflexive voiding</li> </ul>
Urinary calculi	<ul style="list-style-type: none"> <li>• Treat and remove bladder stones</li> <li>• Treat all obstructing calculi</li> <li>• Treat renal calculi if staghorn</li> </ul>
Urinary catheterization	<ul style="list-style-type: none"> <li>• Consider changing indwelling catheter to intermittent catheterization</li> <li>• Consider hydrophilic catheter when performing CIC</li> </ul>
Neurogenic bowel	<ul style="list-style-type: none"> <li>• Promote regular bowel program</li> </ul>

## REFERENCES

1. Devivo MJ: Epidemiology of traumatic spinal cord injury: trends and future implications. *Spinal Cord* 2012; **50**: 365.
2. Jain NB, Ayers GD, Peterson EN et al: Traumatic spinal cord injury in the United States, 1993-2012. *JAMA* 2015; **313**: 2236.
3. Myers JB, Lenherr SM, Stoffel JT et al: Patient reported bladder related symptoms and quality of life after spinal cord injury with different bladder management strategies. *J Urol* 2019; **202**: 574.
4. Cameron AP, Lai J, Saigal CS et al: Urological surveillance and medical complications after spinal cord injury in the United States. *Urology* 2015; **86**: 506.
5. Welk B, Liu K, Winick-Ng J et al: Urinary tract infections, urologic surgery, and renal dysfunction in a contemporary cohort of traumatic spinal cord injured patients. *Neurourol Urodyn* 2017; **36**: 640.
6. Stillman MD, Barber J, Burns S et al: Complications of spinal cord injury over the first year after discharge from inpatient rehabilitation. *Arch Phys Med Rehabil* 2017; **98**: 1800.
7. Manack A, Motsko SP, Haag-Molkenteller C et al: Epidemiology and healthcare utilization of neurogenic bladder patients in a US claims database. *Neurourol Urodyn* 2011; **30**: 395.
8. Crescenze IM, Myers JB, Lenherr SM et al: Predictors of low urinary quality of life in spinal cord injury patients on clean intermittent catheterization. *Neurourol Urodyn* 2019; **38**: 1332.
9. Stamm AW, Adelstein SA, Chen A et al: Inconsistency in the definition of urinary tract infection after intravesical botulinum toxin A injection: a systematic review. *J Urol* 2018; **200**: 809.
10. Gupta K, Hooton TM, Naber KG et al: International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011; **52**: e103.
11. Naber KG, Bergman B, Bishop MC et al: EAU Guidelines for the Management of Urinary and Male Genital Tract Infections. Urinary Tract Infection (UTI) Working Group of the Health Care Office (HCO) of the European Association of Urology (EAU). *Eur Urol* 2001; **40**: 576.
12. Averbeck MA, Rantell A, Ford A et al: Current controversies in urinary tract infections: ICI-RS 2017. *Neurourol Urodyn* 2018; **37**: S86.
13. Groen J, Pannek J, Castro Diaz D et al: Summary of European Association of Urology (EAU) Guidelines on Neuro-Urology. *Eur Urol* 2016; **69**: 324.
14. Allen-Bridson K, Pollock D and Gould CV: Promoting prevention through meaningful measures: improving the Centers for Disease Control and Prevention's National Healthcare Safety Network urinary tract infection surveillance definitions. *Am J Infect Control* 2015; **43**: 1096.
15. Averich TD, Stoffel JT, Goldman HB et al: AUA White Paper on Catheter Associated Urinary Tract Infections: Definitions and Significance in the Urological Patient. *Urol Pract* 2015; **2**: 321.
16. Hooton TM, Bradley SF, Cardenas DD et al: Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis* 2010; **50**: 625.
17. National Healthcare Safety Network: Surveillance for Urinary Tract Infections: Catheter-Associated Urinary Tract Infection (CAUTI) and non-catheter-associated Urinary Tract Infection (UTI) and other Urinary System Infection (USI). Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/nhsn/acute-care-hospital/cauti/index.html>.
18. Nicolle LE: Updated guidelines for screening for asymptomatic bacteriuria. *JAMA* 2019; **322**: 1152.
19. Goetz LL, Cardenas DD, Kennelly M et al: International Spinal Cord Injury Urinary Tract Infection Basic Data Set. *Spinal Cord* 2013; **51**: 700.
20. Cameron AP, Rodriguez GM, Gursky A et al: The severity of bowel dysfunction in patients with neurogenic bladder.



- J Urol 2015; **194**: 1336.
21. Massa LM, Hoffman JM and Cardenas DD: Validity, accuracy, and predictive value of urinary tract infection signs and symptoms in individuals with spinal cord injury on intermittent catheterization. *J Spinal Cord Med* 2009; **32**: 568.
  22. Goodes LM, King GK, Rea A et al: Early urinary tract infection after spinal cord injury: a retrospective inpatient cohort study. *Spinal Cord* 2020; **58**: 25.
  23. Yoon SB, Lee BS, Lee KD et al: Comparison of bacterial strains and antibiotic susceptibilities in urinary isolates of spinal cord injury patients from the community and hospital. *Spinal Cord* 2014; **52**: 298.
  24. Hung EW, Darouiche RO and Trautner BW: *Proteus* bacteriuria is associated with significant morbidity in spinal cord injury. *Spinal Cord* 2007; **45**: 616.
  25. Shekelle PG, Morton SC, Clark KA et al: Systematic review of risk factors for urinary tract infection in adults with spinal cord dysfunction. *J Spinal Cord Med* 1999; **22**: 258.
  26. Vasudeva P and Madersbacher H: Factors implicated in pathogenesis of urinary tract infections in neurogenic bladders: some revered, few forgotten, others ignored. *Neurourol Urodyn* 2014; **33**: 95.
  27. Kennelly M, Thiruchelvam N, Averbeck MA et al: Adult neurogenic lower urinary tract dysfunction and intermittent catheterisation in a community setting: risk factors model for urinary tract infections. *Adv Urol* 2019; **2019**: 2757862.
  28. Lapidus J, Diokno AC, Silber SJ et al: Clean, intermittent self-catheterization in the treatment of urinary tract disease. *J Urol* 1972; **107**: 458.
  29. Bakke A, Digranes A and Hoisaeter PA: Physical predictors of infection in patients treated with clean intermittent catheterization: a prospective 7-year study. *Br J Urol* 1997; **79**: 85.
  30. Krebs J, Bartel P and Pannek J: Residual urine volumes after intermittent catheterization in men with spinal cord injury. *Spinal Cord* 2013; **51**: 776.
  31. Kavanagh A, Baverstock R, Campeau L et al: Canadian Urological Association Guideline: Diagnosis, Management, and Surveillance of Neurogenic Lower Urinary Tract Dysfunction—Full Text. *Can Urol Assoc J* 2019; **13**: E157.
  32. Seki N, Masuda K, Kinukawa N et al: Risk factors for febrile urinary tract infection in children with myelodysplasia treated by clean intermittent catheterization. *Int J Urol* 2004; **11**: 973.
  33. Allio BA and Peterson AC: Urodynamic and physiologic patterns associated with the common causes of neurogenic bladder in adults. *Transl Androl Urol* 2016; **5**: 31.
  34. Bellucci CH, Wollner J, Gregorini F et al: Acute spinal cord injury—do ambulatory patients need urodynamic investigations? *J Urol* 2013; **189**: 1369.
  35. Cameron AP, Campeau L, Brucker BM et al: Best practice policy statement on urodynamic antibiotic prophylaxis in the non-index patient. *Neurourol Urodyn* 2017; **36**: 915.
  36. Stoffel JT: Detrusor sphincter dyssynergia: a review of physiology, diagnosis, and treatment strategies. *Transl Androl Urol* 2016; **5**: 127.
  37. Bacsu CD, Chan L and Tse V: Diagnosing detrusor sphincter dyssynergia in the neurological patient. *BJU Int*, suppl., 2012; **109**: 31.
  38. Gao Y, Danforth T and Ginsberg DA: Urologic management and complications in spinal cord injury patients: a 40- to 50-year follow-up study. *Urology* 2017; **104**: 52.
  39. Lane GI, Roberts WW, Mann R et al: Outcomes of renal calculi in patients with spinal cord injury. *Neurourol Urodyn* 2019; **38**: 1901.
  40. Assimos D, Krambeck A, Miller NL et al: Surgical Management of Stones: American Urological Association/Endourological Society Guideline, PART I. *J Urol* 2016; **196**: 1153.
  41. Patel DP, Herrick JS, Stoffel JT et al: Reasons for cessation of clean intermittent catheterization after spinal cord injury: results from the Neurogenic Bladder Research Group spinal cord injury registry. *Neurourol Urodyn* 2020; **39**: 211.
  42. Prieto J, Murphy CL, Moore KN et al: Intermittent catheterisation for long-term bladder management. *Cochrane Database Syst Rev* 2014; CD006008.
  43. Rognoni C and Tarricone R: Intermittent catheterisation with hydrophilic and non-hydrophilic urinary catheters: systematic literature review and meta-analyses. *BMC Urol* 2017; **17**: 4.
  44. Saadat SH, Shepherd S, Van Asseldonk B et al: Clean intermittent catheterization: single use vs. reuse. *Can Urol Assoc J* 2019; **13**: 64.
  45. Krassioukov A, Cragg JJ, West C et al: The good, the bad and the ugly of catheterization practices among elite athletes with spinal cord injury: a global perspective. *Spinal Cord* 2015; **53**: 78.
  46. Hennessey DB, Kinnear N, MacLellan L et al: The effect of appropriate bladder management on urinary tract infection rate in patients with a new spinal cord injury: a prospective observational study. *World J Urol* 2019; **37**: 2183.
  47. Kang MS, Lee BS, Lee HJ et al: Prevalence of and risk factors for multidrug-resistant bacteria in urine cultures of spinal cord injury patients. *Ann Rehabil Med* 2015; **39**: 686.
  48. Stoffel JT, Van der Aa F, Wittmann D et al: Neurogenic bowel management for the adult spinal cord injury patient. *World J Urol* 2018; **36**: 1587.
  49. Christensen P, Andreassen J and Ehlers L: Cost-effectiveness of transanal irrigation versus conservative bowel management for spinal cord injury patients. *Spinal Cord* 2009; **47**: 138.
  50. Emmanuel A, Kumar G, Christensen P et al: Long-term cost-effectiveness of transanal irrigation in patients with neurogenic bowel dysfunction. *PLoS One* 2016; **11**: e0159394.
  51. Pruss H, Tedeschi A, Thiriout A et al: Spinal cord injury-induced immunodeficiency is mediated by a sympathetic-neuroendocrine adrenal reflex. *Nat Neurosci* 2017; **20**: 1549.
  52. Lucin KM, Sanders VM and Popovich PG: Stress hormones collaborate to induce lymphocyte apoptosis after high level spinal cord injury. *J Neurochem* 2009; **110**: 1409.
  53. Biering-Sorensen F, Bagi P and Hoiby N: Urinary tract infections in patients with spinal cord lesions: treatment and prevention. *Drugs* 2001; **61**: 1275.
  54. Everaert K, Lumen N, Kerckhaert W et al: Urinary tract infections in spinal cord injury: prevention and treatment

- guidelines. *Acta Clin Belg* 2009; **64**: 335.
55. Pannek J and Wollner J: Management of urinary tract infections in patients with neurogenic bladder: challenges and solutions. *Res Rep Urol* 2017; **9**: 121.
  56. Dinh A, Davido B, Duran C et al: Urinary tract infections in patients with neurogenic bladder. *Med Mal Infect* 2019; **49**: 495.
  57. Dinh A, Toumi A, Blanc C et al: Management of febrile urinary tract infection among spinal cord injured patients. *BMC Infect Dis* 2016; **16**: 156.
  58. Linsenmeyer TA: Catheter-associated urinary tract infections in persons with neurogenic bladders. *J Spinal Cord Med* 2018; **41**: 132.
  59. Darouiiche RO, Al Mohajer M, Siddiq DM et al: Short versus long course of antibiotics for catheter-associated urinary tract infections in patients with spinal cord injury: a randomized controlled noninferiority trial. *Arch Phys Med Rehabil* 2014; **95**: 290.
  60. Bleidorn J, Hummers-Pradier E, Schmiemann G et al: Recurrent urinary tract infections and complications after symptomatic versus antibiotic treatment: follow-up of a randomised controlled trial. *Ger Med Sci* 2016; doi: 10.3205/000228.
  61. Kronenberg A, Butikofer L, Odutayo A et al: Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomised, double blind trial. *BMJ* 2017; **359**: j4784.
  62. Chew AB, Suda KJ, Patel UC et al: Long-term prescribing of nitrofurantoin for urinary tract infections (UTI) in veterans with spinal cord injury (SCI). *J Spinal Cord Med* 2019; **42**: 485.
  63. Salomon J, Denys P, Merle C et al: Prevention of urinary tract infection in spinal cord-injured patients: safety and efficacy of a weekly oral cyclic antibiotic (WOCA) programme with a 2 year follow-up—an observational prospective study. *J Antimicrob Chemother* 2006; **57**: 784.
  64. Morton SC, Shekelle PG, Adams JL et al: Antimicrobial prophylaxis for urinary tract infection in persons with spinal cord dysfunction. *Arch Phys Med Rehabil* 2002; **83**: 129.
  65. Cox L, He C, Bevins J et al: Gentamicin bladder instillations decrease symptomatic urinary tract infections in neurogenic bladder patients on intermittent catheterization. *Can Urol Assoc J* 2017; **11**: E350.
  66. Abrams P, Hashim H, Tomson C et al: The use of intravesical gentamicin to treat recurrent urinary tract infections in lower urinary tract dysfunction. *Neurourol Urodyn* 2017; **36**: 2109.
  67. Huen KH, Nik-Ahd F, Chen L et al: Neomycin-polymyxin or gentamicin bladder instillations decrease symptomatic urinary tract infections in neurogenic bladder patients on clean intermittent catheterization. *J Pediatr Urol* 2019; **15**: 178.
  68. Hess MJ, Hess PE, Sullivan MR et al: Evaluation of cranberry tablets for the prevention of urinary tract infections in spinal cord injured patients with neurogenic bladder. *Spinal Cord* 2008; **46**: 622.
  69. Linsenmeyer TA, Harrison B, Oakley A et al: Evaluation of cranberry supplement for reduction of urinary tract infections in individuals with neurogenic bladders secondary to spinal cord injury. A prospective, double-blinded, placebo-controlled, crossover study. *J Spinal Cord Med* 2004; **27**: 29.
  70. Luis A, Domingues F and Pereira L: Can cranberries contribute to reduce the incidence of urinary tract infections? A systematic review with meta-analysis and trial sequential analysis of clinical trials. *J Urol* 2017; **198**: 614.
  71. Lee BS, Bhuta T, Simpson JM et al: Methenamine hippurate for preventing urinary tract infections. *Cochrane Database Syst Rev* 2012; **10**: CD003265.
  72. Hull R, Rudy D, Donovan W et al: Urinary tract infection prophylaxis using *Escherichia coli* 83972 in spinal cord injured patients. *J Urol* 2000; **163**: 872.
  73. Krebs J, Fleischli S, Stoyanov J et al: Effects of oral immunomodulation therapy on urinary tract infections in individuals with chronic spinal cord injury—a retrospective cohort study. *Neurourol Urodyn* 2019; **38**: 346.
  74. Cheng PJ and Myers JB: Augmentation cystoplasty in the patient with neurogenic bladder. *World J Urol* 2019; doi: 10.1007/s00345-019-02919-z.
  75. Baumgart E and Stoffel JT: The Boari bladder flap: an effective continent stoma for the high-compliance neurogenic bladder. *BJU Int* 2010; **105**: 129.
  76. DeLong J, Tighiouart H and Stoffel J: Urinary diversion/reconstruction for cases of catheter intolerant secondary progressive multiple sclerosis with refractory urinary symptoms. *J Urol* 2011; **185**: 2201.

# Study Questions Volume 39 Lesson 29

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1. A 42-year-old woman with a spinal cord injury has had >5 UTIs in the last year. She had symptoms with each infection and all were culture positive with different organisms. The most significant risk factor contributing to the recurrent UTIs is
  - a. an indwelling urethral catheter
  - b. bladder compliance 30 cc/cm H<sub>2</sub>O on urodynamics
  - c. a 0.4 cm non-obstructing renal calculi
  - d. transanal irrigation program for neurogenic bowel
2. A 26-year-old man with a spinal cord injury who performs intermittent catheterization has new onset of urinary incontinence, severe spasticity, loss of upper extremity strength and a temperature of 99° F. A culture shows >100,000 gram-negative bacteria. He has not been hospitalized and does not report chronic UTIs. The culture has not yet identified the specific organism. He has no allergies. You choose to treat him for a UTI. The recommended treatment is
  - a. ciprofloxacin 500 mg twice daily for 14 days
  - b. ciprofloxacin 500 mg twice daily for 7 days
  - c. nitrofurantoin twice daily for 14 days
  - d. trimethoprim 100 mg twice daily for 7 days
3. A 21-year-old woman experienced a T10 spinal cord injury 2 months prior. She was initially managed with a suprapubic tube with no complications. She now wishes to change to intermittent catheterization but is concerned about urinary tract infections. The intervention associated with the highest probability of successful prophylaxis against UTI is
  - a. drinking cranberry juice cocktail daily
  - b. methenamine salts 1 gm twice daily
  - c. performing intermittent catheterization twice daily
  - d. using single use, hydrophilic catheters to keep bladder volumes under 400 ml.
4. A 66-year-old man with a spinal cord injury reports >10 UTIs per year with positive cultures and symptoms of increased urinary incontinence and spasticity. He has had an indwelling urethral catheter since his injury 12 years ago. He has significant soft tissue destruction of his glans penis and his urethra is eroded to the penile-scrotal junction. He has a body mass index of 32 and a large abdominal fold over his suprapubic region. He also has a sacral decubitus ulcer from the overflow incontinence when the catheter frequently obstructs. Urodynamics is performed and he has a capacity of 400 cc, a compliance of 28 cc/cm H<sub>2</sub>O and no detrusor overactivity. The next step is
  - a. nitrofurantoin 100 mg daily for 6 months
  - b. gentamicin 28 gm/60 cc saline washes daily
  - c. suprapubic tube and daily methenamine salts
  - d. continent stoma with a bladder augmentation
5. A 29-year-old with a SCI performs intermittent catheterization every 4-6 hours daily. He has intermittent, foul smelling urine every few days. His urine is clear and he has no additional constitutional symptoms. A urine culture is performed and shows > E. coli 100,000 cfu, pan sensitive. The next step is
  - a. fosfomycin 6 gm po × 1 dose
  - b. ciprofloxacin 500 mg po bid × 10 days
  - c. nitrofurantoin 100 mg po bid × 7 days
  - d. do not treat