

**LOWERING
URINARY TRACT
INFECTIONS
ASSOCIATED
WITH URETHRAL
PROCEDURES**

**Reducing UTIs Associated
with Urethral Procedures:
Concepts and Strategies**

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**QUESTIONS AND ANSWERS ON CLINICAL
PRACTICE RECOMMENDATIONS**

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Reducing UTIs Associated with Urethral Procedures: Concepts and Strategies

Urinary tract infections (UTIs) are a common iatrogenic complication of diagnostic and therapeutic procedures involving urethral manipulation, such as catheterization or cystoscopy. Due to the potential for UTIs to incur additional healthcare costs, adversely affect outcome, and diminish patient satisfaction, steps to reduce risk are warranted in both males and females. Simple steps surrounding the performance of endourethral procedures, such as employing antimicrobial prophylaxis and minimizing injury and trauma to the urethral endothelium through lubricants and anaesthesia, offer opportunities to reduce the risk of infection over that provided by standard infection control practice alone. Many of these steps are well known but applied inconsistently. In performing diagnostic or therapeutic procedures involving the urethra, rigorously implemented UTI risk reduction assures high standards of quality of care.

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Background

In Canada and elsewhere, urinary tract infections (UTIs) are recognized as the single most common infection acquired in the course of healthcare.¹ In studies conducted in the United States, UTIs represent 40% of nosocomial infections.² Although most healthcare-associated UTIs are asymptomatic,³ particularly those acquired in an acute care facility, these pose an important risk of significant complications, including urethral inflammation, strictures, and urolithiasis.⁴ Infection can affect tissue in any part of the urinary tract, including the bladder and kidneys, requiring prolonged and costly courses of antibiotics.⁵ Approximately 20% of potentially fatal nosocomial bacteremias arise from a UTI.⁶

More urgent and comprehensive strategies to avoid UTIs should be considered a priority. Due to the frequency of asymptomatic UTIs and the risk of invasive pathogens and extensive involvement

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when diagnosis is delayed, effective methods of prophylaxis represent the best opportunity to reduce complications, costs, and patient discomfort. When performing a procedure involving urethra, there are two keys steps: infection control and minimizing injury and trauma to the vulnerable urethral epithelium.

Of procedures capable of precipitating healthcare-associated UTIs, urethral catheterization is the most commonly performed and implicated. These devices, commonly called Foley catheters, which pass through the urethra to drain the bladder, are employed in up to 25% of patients at some point during an acute hospitalization.⁷ In one recent survey of 183 acute care hospitals, the rate of hospital-acquired infections in catheterized patients was nearly double that of patients without a device (39.2% vs. 22.9%; $P < 0.001$).⁸ The risk of catheter-associated (CA) bacteriuria is time related with an estimated incidence ranging from 3% to 9% per day.^{9,10} UTIs also appear more likely to involve the bladder, kidney, or other structures when prolonged. In an autopsy study conducted among patients who died in a long-term care facility, the prevalence of chronic pyelonephritis was 10% among those catheterized for >90 days and 0% for those catheterized <90 days in the last year of their life ($P = 0.02$).¹¹

The morbidity from a healthcare-related UTI induces a high cost. In acute care facilities, the increase in average length of stay for a CA-UTI

ranges from 0.4 days in asymptomatic patients to 2 days in those with symptoms.¹² Due to the frequency of this complication, these prolonged stays impose a substantial increase in the cost of management.¹³ The increased cost of care is accompanied by a diminished quality of life in those who develop symptoms.¹⁴ Nosocomial UTIs produced by other procedures involving the urethra are likely to impose similar morbidity, providing a rationale for developing formal strategies to reduce UTI risk from any cause.

Mechanism

Even in otherwise healthy individuals, UTIs are common when the balance of resident microorganisms important to preventing infection is lost.¹⁵ As a result, the substantial risks of infection from procedures that involve manipulation of the urethra are not surprising. Although the healthy urinary tract is normally sterile,¹⁶ the epithelium of the urethral lumen is highly vulnerable to injury, setting the stage for pathogen adherence and invasion. Moreover, vulnerability to infection from urethral manipulation is exacerbated by the proximity of the urethral orifice to perianal and perivaginal colonies of microorganisms.¹⁷ In those seeking healthcare, this vulnerability may be further exacerbated by a diminished immune response secondary to the underlying illness.

Healthcare-acquired UTIs are uncommon in the absence of invasive procedures that involve the urethra, providing a focus for efforts to reduce this complication. The mechanisms of these infections, and therefore the opportunities for prevention, are straightforward. Resident bacteria on the skin and within the urethral lumen have the potential to be disturbed by invasive procedures, and the risk of devices carrying an inoculum of bacteria into the urethral lumen is underscored by the pathogens typically isolated. Consistent with the ability of otherwise benign bacteria to become invasive when placed in environments where natural mechanisms of inhibition are lost,¹⁸ approximately two-thirds of bacteria associated with CA-UTIs can be traced to an extraluminal origin.¹⁹

Invasive procedures have the potential to disrupt the otherwise highly effective innate immune defenses at work in the urinary tract.

Furthermore, invasive procedures have the potential to disrupt the otherwise highly effective innate immune defenses at work in the urinary tract. These defenses serve to prevent bacteria and other microorganisms from the initial steps of infection, such as adherence to epithelial cells,

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through expression of antimicrobial chemokines and upregulation of phagocytes.²⁰ When devices irritate the epithelium, the transition to an adaptive immune response, which features upregulation of inflammatory signaling, may be better suited to responding to an existing infection than preventing an infection from occurring.

Due to these factors, any diagnostic or therapeutic procedure that involves penetration of the urethra incurs a potential infection risk. This includes insertion of cystoscopes, catheters, or other devices employed in the evaluation or treatment of conditions involving the urinary tract. For indwelling catheters, the risks are multiplied. Initially and over time, the catheter entry point at the urethral meatus provides a route for migration of pathogens into the urethra.²¹ In addition, biofilm that develops on catheters provides a medium for growth.²² Biofilm, which inhibits the effect of antimicrobial agents,²³ also fosters resistant infections due to the ability of colonizing bacteria to effectively communicate genetic information during localized growth.²⁴ These differences in the patterns of contamination and growth explain why CA-UTI pathogens associated with biofilm are often more virulent than those isolated from UTIs stemming from other sources.

These mechanisms provide clear targets for prevention. In addition to sterile technique, the urethral epithelium must be protected from injury and stress. One step is to use lubricants to reduce friction as catheters, cystoscopes, or other instruments are inserted. Another is to provide anesthesia to reduce pain responses and

stimulation of inflammatory mediators. The goal is not only to prevent bacteria from entering the urethral lumen but reducing the risk of adherence essential for infection when sterile technique is imperfect.

Steps to Lower Risk

The best strategy for avoiding healthcare-related UTIs stemming from procedures involving the urethra is to reduce the number of procedures performed. Strategies include non-invasive diagnostic evaluations, such as ultrasound, and avoiding urethral catheterization when other means of voiding are feasible. Several studies have provided evidence that urethral catheterization is employed excessively, particularly among the elderly.^{25, 26, 27} Initiatives to limit these procedures have been advocated in order to reduce morbidity and healthcare costs,²⁸ even though a survey of hospitals in the United States suggests that few acute care facilities have implemented active programs.²⁹

When invasive procedures are unavoidable, several recommendations for reducing the risk of CA-UTIs have been provided in guidelines from the Infectious Diseases Society of America (IDSA).¹³ These include ensuring that there is a clear indication for catheterization, formally training staff about catheter placement technique, establishing aseptic technique policies, and monitoring patients for infection. The importance of rigorous application of well-established infection control practices, such as hand washing and environmental cleanliness, cannot be over emphasized. The ability of evidence-based infection

TABLE 1 | Urinary Catheter Lubricants

CHARACTERISTICS	LIDOCAINE JELLY (Xylocaine®)	LIDOCAINE JELLY (Cathejell®)	LIDOCAINE AND CHLORHEXIDINE GEL (Instillagel®)
Lubricant	✓	✓	✓
Anesthetic	✓ (lidocaine 2%)	✓ (lidocaine 2%)	✓ (lidocaine 2%)
Antiseptic	No	No	✓ (chlorhexidine 0.05%)
Available sizes	10 mL pre-filled syringes	12.5 mL pre-filled syringes	6 mL and 11 mL pre-filled syringes
Available in hospitals	✓	✓	✓
Assembly required	✓	No	No
Available OTC in community pharmacies	No	✓	✓
Administration device	Single-use syringe	Collapsible, single-use syringe	Single-use syringe

control practices to reduce nosocomial infection risk, including risk of UTI, is well documented.³⁰

For specifically preventing healthcare-associated UTIs stemming from urethral manipulation beyond routine infection control strategies, two factors deserve attention. The first is providing antisepsis in the urethra. The other is avoiding irritation to the urethral epithelium. Although inflammation is a common consequence of infection, urethritis may also lower the innate epithelial defenses against adhesion of bacteria required for colonization and invasion. Pain control may also be important. Although pain arises from inflammation, there is at least experimental evidence to suggest that pain signaling upregulates prostaglandins and other mediators of the inflammatory response,³¹ which may increase susceptibility of the urethral epithelium to bacterial adhesion and invasion.

Antisepsis, lubrication, and pain control provide the pillars of UTI prevention when performing invasive procedures involving the urethra. In guidelines from the IDSA for prevention of CA-UTIs, antimicrobial-coated catheters are identified as a potential strategy and systemic antimicrobials are recommended specifically.¹³ In addition, insertion with aseptic technique and sterile equipment is also a specific IDSA recommendation. The additional value of lubrication and pain control when inserting catheters or other endourethral devices is supported by an extensive literature developed over more than 20 years. Many studies were performed with a product that combines lidocaine as an analgesic and chlorhexidine as an antiseptic. Lubricating ingredients such as propylene glycol have been added to reduce risk of epithelial damage from device insertion (Table 1).

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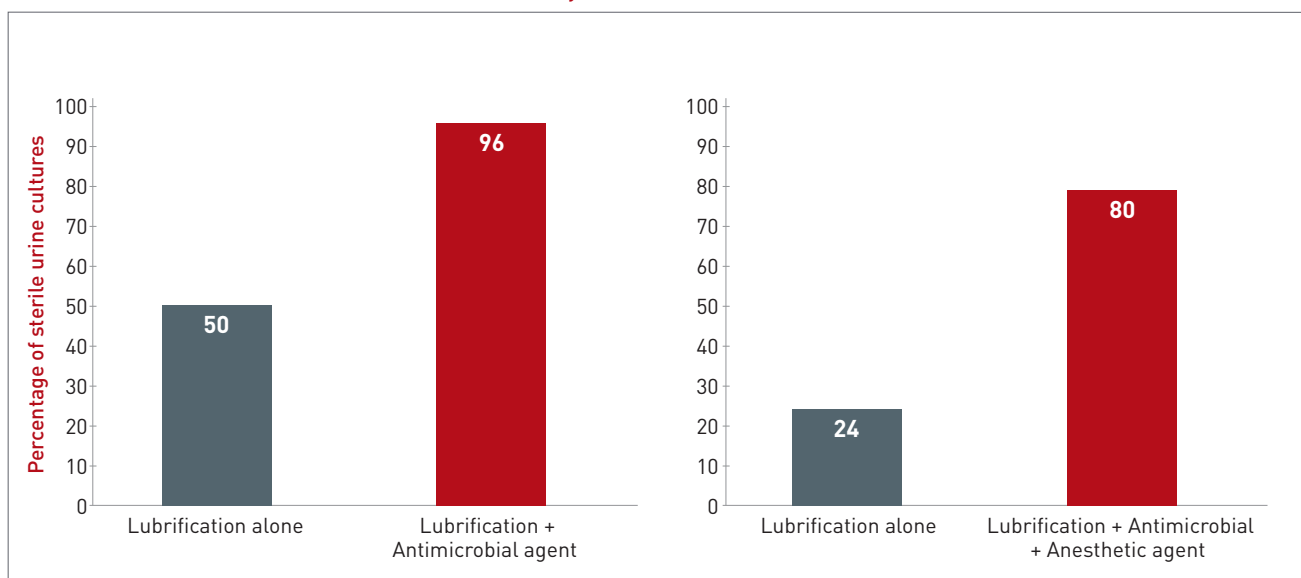
The published clinical studies with this combination lidocaine and chlorhexidine agent, which is indicated for surface anesthesia, lubrication, and antisepsis for females and males undergoing cystoscopy, catheter insertion, and other endourethral procedures, employ a variety of efficacy and safety endpoints but include reductions in rate of UTIs. In a study of 149 females undergoing catheter insertion after major gynecologic surgery, the rate of UTI was reduced by 32% in those whose insertion was performed with the combination agent relative to those who were not (20% vs. 13.5%; $P < 0.05$).³² Consistent with other studies performed with this agent, no significant adverse events were reported.

Antisepsis, lubrication, and pain control provide the pillars of UTI prevention when performing invasive procedures involving the urethra.

In a study comparing the lidocaine and chlorhexidine combination agent to liquid paraffin among 320 patients undergoing catheter insertion (135 patients) or cystoscopy (185 patients), the rate of sterile urine cultures was nearly four times higher in the catheter group (80% vs. 24%) and approximately 2 times higher in the cystoscopy group (63% vs. 36%) among those who received the combination agent.³³ Moreover, pain was reported in those patients undergoing cystoscopy who received liquid paraffin but not in those who received the lidocaine and chlorhexidine agent.

In another cystoscopy study of 175 patients comparing the combination agent to two other types of gels without antiseptic activity, sterile urethral smears were obtained in 96% of those receiving the combination product versus 50%

FIGURE 1 | Rate of Sterile Cultures after Urinary Catheter Insertion



Adapted from Vogler H. *Zeitschrift für Urologie und Nephrologie* 1980;73:401-5; Wabrosch T, Magyar SO, Zoltan EF. *Magyar Urologia* 1990;4:371-75.

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or fewer with the alternative gels (Figure 1).³⁴ Similar results were observed in a comparison of the combination agent to xylocaine.³⁵ In addition to yielding data confirming safety,³⁶ published studies have also associated it with relief of pain.³⁷ In one study, the lubricating effect was shown to prevent microlesions in the urethra,³⁸ a potential mechanism for reducing the risk of both urethritis and UTI.

This literature provides support for the value of a comprehensive approach to endourethral procedures that combines sterile technique with antisepsis, analgesia, and lubrication. When combined, each has the potential to achieve an incremental reduction in risk of UTI by addressing the independent but interrelated risks that increase susceptibility to infection. The additional clinical value of pain prevention and improved ease of inserting devices into the urethra cannot be discounted. This step in care is broadly applicable for any healthcare-related procedure involving penetration of the urethra, including self-

catheterization performed by patients outside of the hospital setting. The value of antisepsis, analgesia, and lubrication should be considered in the context of other recommended steps in UTI prophylaxis.

Conclusion

Due to an exceptional representation among nosocomial infections, UTIs are regarded as an important focus of infection control strategies designed to reduce healthcare-related morbidity and costs. A large proportion of nosocomial UTIs are attributed to penetration of the urethra for diagnostic or therapeutic procedures. A comprehensive and multifaceted approach to UTI prophylaxis in these individuals requires consideration of steps beyond rigorous application of sterile technique. This includes steps to reduce injury to the urethral epithelium in order to sustain its integrity. In the context of other methods of UTI prophylaxis, there is evidence to support an approach that combines antisepsis with pain control and lubrication. ●

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Urologist's Perspective

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Q Healthcare-related UTIs are common, particularly among patients who require endourethral procedures, such as catheterization. Do you feel costs and morbidity could be lowered with more effective prevention?

A Based on multiple surveys that have identified UTIs as the most common type of nosocomial infection, a large literature has emerged outlining strategies to reduce risk. As catheterizations are the most common source of healthcare-related UTIs, this has been the most common focus of efforts toward risk reduction. Not least important, many guidelines and review articles, including the 2009 practice recommendations from the Infectious Diseases Society of America (IDSA) suggest strict indications for urinary catheters in order to restrict use to those who cannot be managed with alternative approaches. In those who do require catheterization or any invasive endourethral procedure, steps to improve sterile technique and address risk factors for pathogen invasion should be considered critical to efforts to reduce the complications imposed by iatrogenic infection. Avoiding UTIs means avoiding the costs of managing a UTI, which can be particularly substantial if a UTI results in a hospital admission or extended length of stay.

Q For endourethral procedures, an antiseptic to eliminate potential pathogens makes sense, but is there potential value for urethral lubrication to reduce the inflammatory response induced by catheters, cystoscopes, or other devices inserted into the urethra?

A There is a relatively small pool of evidence that directly demonstrates a reduction in the risk of UTI when lubrication is employed to facilitate the introduction of a catheter or other device into the urethral canal, but lubrication can reduce discomfort. Certainly, lubrication can be recommended on the basis of a more favorable patient experience. It is reasonable to expect lubrication to reduce trauma from a device passing through the membranous tissue that lines the urethra even if it has not yet been shown specifically that a reduction in the pain response will avoid activation of inflammatory mediators. When lubrication is combined with an antiseptic, there is potential for both to reduce the risk that pathogens will adhere to urethral cells to initiate colonization.

Q What is the potential for anesthetic properties in a lubricating antimicrobial gel to encourage proper technique to lower UTIs?

A The likelihood of achieving a meaningful reduction in the risk of UTIs from endourethral procedures is likely to be dependent on developing a strict and multifaceted protocol. No step may be more important than ensuring a sterile technique. The perigenital region is rich in resident bacteria that are readily converted to pathogens when allowed access to the urinary tract. Introducing catheters and other endourethral devices into the urinary tract with a lubricating gel that combines an antiseptic and an anesthetic should be part of a regimented protocol that includes sterilization of the perigenital region as well as patient education regarding the goals of treatment and the risks of UTI. Patient comfort is not the least important part of a strategy that requires patient cooperation and adherence. Lowering the risk of UTIs associated with endourethral procedures has proven challenging. A comprehensive approach is likely to be instrumental to success.

Obstetrician/Gynaecologist's Perspective

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Q For endourethral procedures, is it attractive to employ gels with both antimicrobial and lubricating properties to reduce a pro-inflammatory insult to the urethral mucus membrane?

A The use of gels for introducing a Foley catheter or any other device into the urethra may be attractive, but it is an empirical practice. There are no well-controlled trials to compare gels with different properties or to compare gels to no gel, but there is a rationale for lubrication to improve patient comfort as well as a rationale for employing a gel with antimicrobial properties to reduce risk of introducing microorganisms into the urinary tract. It can be speculated that lubrication will reduce friction on the mucosal lining of the urethra, a potential risk for modifying host defenses to infection. This may be of even greater benefit to the delicate mucosa in postmenopausal women. It is often difficult to avoid vagina flora contaminating an endourethral procedure in females; a gel with antimicrobial properties is a reasonable strategy within other steps to prevent UTI.

Q Gels with anesthetic activity would be expected to improve the experience for patients undergoing endourethral procedures but could these gels also ease insertion and thereby preserve the integrity of the mucus membrane?

A Again, there is a rationale for empirical use of a lubricating gel with anesthetic activity to improve patient comfort. The value of a gel that includes a mild topical anesthetic to reduce risk of injury to the mucosa, thereby reducing risk of UTI, has not been evaluated objectively, so no definitive answer can be provided regarding clinical benefit, but such an approach may be reasonable for the potential benefits added to the primary objective of improving patient comfort. My experience of endourethral procedures in an awake patient is largely limited to pregnant and post-partum women experiencing difficulty voiding. A lubricating gel in itself would help preserve the integrity of the mucosa and also decrease discomfort, but the additional comfort from a mild topical anesthetic would be of benefit in these situations.

Q For patients who perform self-catheterization, can lubrication gels that combine antiseptics and anesthesia improve the experience as well as be part of a strategy to reduce infection risk?

A Many patients performing self-catheterization are likely to prefer a lubricating gel for its role in easing insertion of the device. Patients may also gravitate toward a gel that offers topical analgesia to reduce discomfort and appreciate the potential of antimicrobial action to reduce risk of UTI. Caution would be advised to patients on the use of anesthetic gels in self-catheterization. First, sensory feedback is useful to insert the catheter in the correct location and at the correct angle. Lack of sensation in a person who is not completely familiar with the procedure may lead to unintentional urethral injury. A lubricating gel that also has antimicrobial properties would be more attractive in this setting as the anatomic location of the urethra can make it difficult to maintain a sterile field and still manipulate the catheter properly. Clinical trials are needed to advocate these gels on an evidence basis, but in certain circumstances patients may find reassurance in lubricating gels with properties that offer additional potential benefits.

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Surgeon's Perspective

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Q Many patients require an indwelling urinary catheter after surgery. Does the surgeon have a role in encouraging strategies to reduce risk of UTIs in these patients?

A Of course, the surgeon should be concerned about all aspects of preoperative and postoperative care that has a potential impact on outcome, but increasing emphasis on quality of care documentation is requiring even more attention to complications such as UTIs. For surgeons and hospitals to lower their complication rate, it is essential that everyone get on board with protocols, care pathways, and other strategies that increase the rigor with which preventive steps are implemented. Surgeons should be aware of which patients have been catheterized and to understand the protocols being employed to reduce the high risk of UTIs in these individuals.

Q Clearly, sterile technique is important for reducing UTI in anyone undergoing an endourethral procedure, not just catheterization, but is there a rationale for reducing UTI risk by adding antimicrobial and anesthetic properties to lubricating gels?

A It is not surprising that introducing a catheter or any other foreign body into the urethral canal is associated with a high rate of infection. Foreign bodies provide a ready vector for facilitating transport or migration of the bacteria and other microbes that commonly colonize the perigenital area to mucosal membranes of the urinary tract. Lubricating gels are often used to reduce discomfort and reduce trauma from endourethral procedures. Adding a mild anesthetic is conceptually attractive. First of all, it may further reduce discomfort relative to lubrication alone. In addition, a reduction in pain may avoid upregulation of inflammatory mediators involved in tissue irritation that may contribute to susceptibility for infection. However, from my perspective, the two most important steps to reduce UTIs in patients who require a catheter is rigorous sterile technique and early removal.

Q In surgical patients, do you feel that prevention of nosocomial UTIs should be the focus of a multidisciplinary approach that involves not only surgeons, but urologists, nurses and other healthcare personnel who employ care pathways that encourage risk reduction?

A For rigorously reducing the risk of UTIs, I think the challenge for surgeons and perhaps for others involved in the care of the surgical patient is not accepting that some proportion of infections are inevitable. Surgeons should not only be involved in making sure that urinary catheterization is necessary, which may be one of the most important steps for reducing UTI risk, but, as stated in the answer to the first question, verify that steps are being taken to reduce infection risk when a catheter is placed. For surgical patients, preventing UTIs is traditionally left to nursing staff or urologist consults, but optimal outcomes depends on collaboration that ensures that everyone is rowing in the same direction.