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Prevention of Urinary Tract Infections in the Outpatient and Inpatient Settings

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Additional information is available at the end of the chapter

1. Introduction

Urinary tract infections (UTIs) are one of the most common health problems plaguing women. About half of women will experience a UTI during their lifetime. The incidence is much lower in men but increases with age. In patients over the age of 65, at least 20% of women and 10% of men have bacteruria [1]. The incidence also increases with hospitalization or institutionalization. UTIs are the most common nosocomial infection, and more than 80% of these are associated with an indwelling catheter [2]. There is also a higher risk of UTIS in pregnancy and some chronic diseases including diabetes, multiple sclerosis, spinal cord injuries or disease, and immunosuppressive diseases such as HIV.

The cost of treating UTIs is substantial both in inpatient and outpatient settings. In the United States in the year 2007, approximately 2.47 billion dollars were spent on outpatient treatment of UTI and this excluded spending on prescriptions [3]. The estimated cost of nosocomial UTIS is approximately 2.66 billion dollars in 2007 dollars [4]. There are simple and effective measures for prevention of UTIs which can significantly limit morbidity and cost, but these are often overlooked,

Certain patients, particularly women, despite having normal anatomy and function of the urinary tract, are genetically predisposed to urinary tract infections. This tendency seems to be related to variations in the urinary tract epithelium and it's interaction with bacteria. Once a person has a UTI, he or she is more likely to get another within a year. Recurrence rates in women vary from 28 to 82%, with higher rates seen in women with a prior history of UTI [5]. The risk of recurrent UTIs increases with higher number of prior infections. It also decreases with a longer time interval between the first and second infections. [4] However, even with long intervals between infections, about one sixth of women have difficulties with recurrent infections throughout their lifetime [4]. Preventive strategies should be targeted to this group.

2. Prevention of UTIS in the outpatient setting

Given the increasing emergence of multidrug resistant bacteria in UTIs, every effort should be made to use non-pharmacologic measures as first line preventive strategies in patient who have recurrent UTIs.

2.1. Hygiene

There are many “old wives” tales about causes of UTIs, and many of these beliefs are ingrained in women. Women are told by other women to wear cotton underwear, avoid drinking sodas, and even to avoid strong laundry detergent in an effort to prevent UTIS.

Studies have not been done to evaluate most of these measures. A search of PubMed using the terms “urinary tract infection” and “sodas, carbonated beverages, hygiene, wiping patterns” did not reveal any studies. However, it is intuitive that girls and women should always wipe from front to back after a bowel movement to avoid bringing fecal bacteria towards the vagina and the urethra. If a woman is predisposed to urinary tract infections, she should carefully watch hygiene. It is helpful to show these women a picture of the vulvar anatomy, explaining the close proximity of the urethra to the anal area and that an infection occurs when intestinal bacteria enter the urethra. These women should be encouraged to clean with a moist wipe (such as a baby wipe or other hygienic cleansing wipe) after a bowel movement. It is the author’s opinion that it is helpful to wash the perineum and perianal area with antibacterial soap prior to intercourse. Patients should also be instructed to avoid any sexual practices that might bring colonic bacteria forward towards the vagina, such as touching the perianal area and then the vaginal area. Voiding after intercourse has been shown to protect against UTI [5]. There is no evidence that vaginal douching after intercourse decreases UTI incidence and in fact, it may increase the risk of vaginal infections. As such, it is not a recommended practice.

It is also the author’s opinion that patient with recurrent UTIs should avoid tub baths. This recommendation comes from repeated observations over years of practice that many women who present UTIs give a history of taking frequent tub baths. It is plausible that the hot water washes away some of the protective mucous coating the urethral and vaginal introitus, making the mucosa drier and more susceptible to bacterial colonization. There were no studies on this found during a literature search on PubMed and OVID using the search terms “tub bath” “bathing” and “urinary tract infection”. There were interestingly a few papers in the 70s linking *Pseudomonas* infections, including UTIs, to whirlpools and hot tubs, and this led the Centers for Disease Control (CDC) in the United States to establish standards for chlorination and filtration of these tubs [6]. Patient with UTIs should likely avoid these public tubs as well. Even if the water is correctly chlorinated and filtered, it is extremely hot and drying to the skin.

2.2. Diet

There is evidence that links overactive bladder but not UTI to regular consumption of carbonated beverages. A large study that examined the prevalence and incidence of irritative voiding symptoms in men and women over a 12 months period showed a significant associ-

ation between onset of overactive bladder and weekly consumption of carbonated drinks. ($P=.03$). These findings did not apply to men in the survey [7]. There are also several studies linking caffeine to lower urinary tract symptoms, but not infection [8], [9].

Although these data don't indicate that dietary factors actually cause UTIS, women who have frequent UTIs often mistake the frequency and urgency caused by a dietary bladder irritant for an infection. This could lead to calls to their provider requesting therapy and the chance of overtreatment. Thus it would seem prudent for these women who are plagued with frequent UTIS to avoid an excessive amount of carbonated beverages and caffeine. There may well be other dietary bladder irritants, such as citrus and other acidic fruits that can cause urgency. It is helpful for women with frequent UTIS to keep a food diary for a short time and see if they can link certain foods to irritative voiding symptoms.

2.3. Contraception

Although there are no contraceptive methods that prevent UTIs, there are several that may increase the risk, primarily diaphragms and spermicides. Diaphragms were widely used in the 1950s through the early 1980s, but are not often used now that there are more effective methods of contraception that are easier to use. Diaphragm users have been shown to have a two to threefold increased risk of UTI compared to non-users [10], [11]. This is due to partial urethral compression by the rim of the diaphragm and also is likely related to the spermicide that is used on the rim.

Spermicides contain nonoxynol-9 which can cause a chemical irritation to the vaginal and urethral mucosa as well as changes in the normal flora. This in turn predisposes to colonization by coliforms as well as *Staph saprophyticus* [12]. Patients with recurrent UTIs should avoid diaphragms and spermicide coated condoms, as well as other barrier agents containing nonoxynol-9 such as foam, suppositories, and sponges.

2.4. Vaginal estrogen replacement for postmenopausal women

After menopause, the vulvar skin atrophies and thins. There is decreased blood flow to this area and decreased mucous production. The periurethral mucosa is lubricated by the Skene's glands and these also atrophy, thus causing loss of mucous that is the first line of defense against bacteria. In addition, vaginal pH increases after menopause and lactobacilli counts decrease. These conditions set up the postmenopausal woman for higher risk of UTIs, particularly after intercourse. In addition, urinary incontinence, the presence of a cystocele and incomplete emptying and have been found to be highly associated with recurrent UTI, and these are problems that increase with age as well [13].

Systemic estrogen replacement therapy in the prevention of UTI has not been shown to be of help in preventing recurrent UTIs in postmenopausal women. However, there is strong evidence that *topical vaginal* estrogen replacement does protect against recurrent UTIs. Raz and Stamm in 1993 conducted a randomized controlled trial in postmenopausal women and found a significant decrease in rate of urinary tract infections in the treated group which used intravaginal estrogen twice weekly, versus placebo., (0.5 vs. 5.9 episodes per patient-year,

$P < 0.001$. They demonstrated a return of lactobacilli to the vaginal flora and normalization of vaginal pH. In addition, vaginal colonization with Enterobacteriaceae fell from 67 percent to 31% in the treated group [13].

Vaginal estrogen therapy is available in three forms in the United States. These are listed in decreasing order of systemic absorption:

1. Estradiol vaginal cream: Premarin Vaginal cream = 0.625 mg/gm and Estrace vaginal cream = 0.1 mg/gm. Dosage varies from 0.5 mg to 2 mg/vagina twice weekly. Retail cost is \$140/tube for both of these products (www.drugstore.com)
2. Estradiol vaginal tablets: Vagifem = 10 mcg estrogen per tablet. Dosage is one tablet inserted vaginally twice weekly. Retail cost is \$64.00/month
3. Estradiol 2 mg vaginal ring. One ring is placed intravaginally and changed every 3 months. Retail cost is \$216.00 per ring (3 months).

An exact dosage for vaginal estrogen therapy for UTI prevention hasn't been established. Raz's landmark study used 0.5 mg estriol cream intravaginally once daily for 2 weeks, then twice weekly. Estriol cream is not commercially available in the United States and most prescribers use one to two grams of Estrace or Premarin cream per vagina twice weekly. Dosage should be individualized based on patient weight and degree of atrophy present. In an obese woman with higher levels of endogenous estrogen, 0.5 mg of estrogen cream twice weekly will likely be adequate, whereas in a thin woman who is very atrophic, a higher dose will be needed, especially in the initial months of treatment. Of note, progesterone does not need to be prescribed with topical vaginal estrogen in women with a uterus. In the recommended dosages, vaginal estrogen therapy does not cause endometrial hyperplasia as the amount of systemic absorption of estrogen is quite low. Progesterone therapy does NOT need to be given in a woman with a uterus who is using vaginal estrogen on a long term basis.

Despite strong evidence of benefit, topical estrogen is underutilized as a preventive strategy. In a study of nursing home residents in Norway who were on preventive therapy for UTI, only about 10% were prescribed vaginal estrogen [14]. Many women have a fear of estrogen containing products due to fear of breast or uterine cancer. There is no evidence that vaginal estrogen therapy causes uterine cancer or even endometrial hyperplasia. The same holds true for breast cancer. Patients often need reassurance that vaginal estrogen is safe and doesn't have the risk of systemic ERT, which uses much higher dosages. Vaginal estrogen therapy can be used safely in women with a prior history of breast cancer or thrombosis. The estrogen ring has the lowest amount of systemic absorption, followed by the vaginal estrogen tablets, then cream.

Cost is also significant obstacle in the United States, as many health insurance plans don't cover these products well, and after age 65 there is variable coverage of these with Medicare. One solution for women who cannot afford these products is to have a compounding pharmacist make an equivalent substitute. Estradiol 0.1 mg/gm can be added to a pluronic gel base that has excellent adherence to the vaginal mucosa. Cost is approximately \$50.00 for a two to three month supply.

2.5. Natural remedies

Cranberries and their juice have long been touted for both treatment and prevention of UTI. This was previously thought to be due to acidification of the urine, but more recent research has shown that substances (proanthocyanadins) in the cranberry prevent adhesion of *E. coli* strains to the uroepithelium, including multidrug resistant strains [15]. Studies of cranberry prophylaxis are mixed, but several recent studies have shown that there is benefit from this simple remedy. Wang et al did a meta-analysis of randomized controlled trials comparing prevention of UTIs in users of cranberry products versus placebo or non-placebo controls. They found a risk ratio for cranberry users versus nonusers was 0.62 and statistically significant, leading them to conclude that cranberry products are associated with protection against UTIs. Further, cranberry products were more effective in certain subgroups including women with recurrent UTIs, children, cranberry juice users (as opposed to tablets) and those who used cranberry products more than twice daily [16].

A recent RCT examined women with recurrent UTIs, randomizing them to either cranberry juice or placebo for 6 months. Those in the cranberry juice did have lower incidence of recurrent UTIs, but it did not reach statistical significance. However, they did have significantly decreased counts of P-fimbriated *E. coli* in their urine during the study periods. These are uropathogenic strains with fimbriae capable of attaching to the uroepithelium. The authors concluded that though the cranberry juice didn't significantly reduce the number of recurrent UTIs, the reduction in adherent *E. coli* lends plausibility to a protective effect of cranberry and warrants further large scale studies [17].

Within the pediatric population, several new cranberry studies have emerged. A RCT from Finland randomized 263 children with a prior history of UTI to 6 months of cranberry juice versus placebo. Their findings: the juice did not significantly reduce the number of children who experienced a recurrence of UTI, but it was effective in reducing the actual number of recurrences and related antimicrobial use [18]. Another recent randomized controlled prospective study found cranberry capsules effective in the prevention of UTI in children with neurogenic bladder caused by myelomeningocele who required chronic intermittent catheterization. The median UTI rate in this small cohort of 20 children was 0.5 UTI/year during placebo usage and 0/year with cranberry capsule usage. This decrease was statistically significant. No side effects were noted [19].

Cranberry juice is safe in pregnancy and there is data from a small study to suggest that it may be efficacious in preventing asymptomatic bacteruria and symptomatic UTI. However in this same study, the juice was poorly tolerated by the pregnant women, and there was a high rate of withdrawal [20]. If used in pregnancy, use of cranberry pill form will likely be more effective as compliance will be higher.

Propolis is a resinous material collected by bees from exudates and buds of plants, then mixed with wax and bee enzymes. It has well documented antibacterial activity. Lavigne et al added propolis to proanthocyanidins from the cranberry and studied its effect on human volunteer subjects. They found that once daily ingestion offers some protection against bacterial adhesion, bacterial multiplication and virulence in the urinary tract [21].

Blueberries and blackberries are widely touted on the internet as effective prevention for UTIs but there are no trials of these foods found on PubMed or Ovid. Bearberry leaves are another folk remedy believed to be helpful in treating mild UTIs, but likewise, no studies of effectiveness have been undertaken. The same hold true for Vitamin C. There are no studies of this alone for prevention of UTI. However when Vitamin C was added to cranberry extract, D-mannose, fructo-oligosaccharides, and bromelain, this mixture was effective in reducing recurrent UTIs and improving quality of life in both pre and postmenopausal women [22]. More studies are needed on efficacy of these nutraceuticals.

In summary, there is emerging evidence that cranberries are effective in the prevention of UTI in women and children, including children with neurogenic bladder. Both the juice and the capsules seem to be effective, the juice possibly more so, but it should be unsweetened juice to prevent high intake of unnecessary sugars. The capsules may be better tolerated however, particularly in pregnancy. Whichever form is used, it seems that it should be ingested three or more times daily for maximal effectiveness. The optimal dose of cranberry is not known and was studied in only one of the studies included in Wang's meta-analysis [23]. He concluded that the cranberry juice provides the most benefit, and it should be ingested three times daily at a dose of 4 to 6 ounces [24]. Most over the counter cranberry preparations contain 400 to 500 mg of cranberry extract and are likely also more effective if taken three times/daily. More studies are needed in this area to determine the optimal dose and type of cranberry. Cranberries should be used with caution in patients on blood thinners and those with kidney stones.

2.6. Vaccines

Attempts have been underway to create an oral or parental immunoprophylaxis or vaccination for patients with recurrent UTIs for some time, but these efforts have been frustrated by the short lived nature of immunity created. The premise of a vaccine is inactivated bacteria or bacterial components presented to a host's mucosal surface to boost immunity. Intranasal sprays, sublingual preparations, vaginal suppositories and IM injections have been developed thus far. Recent publications show promise in this area. Currently, a vaccine has been developed by Immunotek in Spain called Uromune® a sublingual preparation which contains an inactivated bacterial cell suspension of selected strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, and *Enterococcus faecalis*. A multicenter observational study was conducted by Lorenzo-Gomez et al in which a group of 319 women with a history of recurrent UTIs were divided into two groups. Group A was treated with 3 months of this vaccine and Group B with 6 months of prophylactic antibiotic treatment with sulfamethoxazole/trimethoprim 200/40 mg/day. These women were then followed for 15 months. The authors found that patients in Group A had a highly statistically significant decrease in number of UTIs that persisted for up to 15 months. The numbers of patients who did not have any UTI at 3, 9, and 15 months were 101, 90, and 55 in group A versus 9, 4, and 0 in group B ($P < 0.0001$) [25].

2.7. Pharmacologic suppressive treatments: Antibacterial

2.7.1. Methenamine hippurate

Methenamine hippurate is not an antibiotic, but is a urinary antibacterial agent used for prevention of recurrent UTI when long term therapy is needed. It exhibits antibacterial activity by conversion of methenamine to formaldehyde in the presence of acidic urine. The hippuric acid component acidifies the urine and also has some antibacterial activity. This drug is often used in combination with a urinary acidifier such as sodium phosphate (Uroqid acid#2). The dose for suppression is 1 gram orally twice daily. It is safe for both adult and pediatric patients, but is contraindicated in patients with renal or hepatic insufficiency. Methenamine is Pregnancy Category C, and there are no adequate and well controlled studies of its use in pregnancy. It is excreted in breast milk and the amount excreted does not appear to adversely affect the nursing infant.

Methenamine is effective in the prevention of recurrent UTIs in both adult and pediatric patients, but should only be used following eradication of the infection by antibiotics. It is not as effective as nitrofurantoin or trimethoprim/sulfamethoxazole as prophylactic treatment, but also does not cause antimicrobial resistance. Per Micromedex, it has shown to be effective in reducing bacteruria in gynecological surgical patients with short term foley catheter placement up to 3 days, but was not effective in prophylaxis for patients with long term indwelling catheters.

Most of the studies of efficacy of methenamine were done in the 1960s and 70's. Lee et al undertook a meta-analysis of all studies in 2007. There were 13 studies included, 6 of which reported on symptomatic UTI and eight for bacteruria. The overall estimates were difficult to interpret due to heterogeneity of the studies. Subgroup analysis did show that methenamine likely has benefit in patients without renal tract abnormalities for both symptomatic UTI and bacteruria but not in patients with known renal tract abnormalities. The authors concluded that methenamine may be effective for preventing UTI in patients without renal tract abnormalities, especially when used for short-term prophylaxis. It doesn't appear to work in patients with neurogenic bladder or those who have renal tract abnormalities. The rate of adverse events is low. There is a need for further large well RCT to clarify the value of its longer term use for patients without renal tract abnormalities [26].

2.8. Pharmacologic suppressive treatments: Antimicrobials

There are 3 strategies commonly used today for prevention for patients with recurrent UTI:

1. Post coital therapy: The patient takes a single dose of an antibiotic immediately after intercourse
2. Patient initiated therapy: The patient takes a single antibiotic tablet on first noticing symptoms of infection
3. Continuous daily suppression: The patient takes a daily dose of suppressive antibiotic for 3 to 6 months or sometimes longer.

Choosing an effective preventive strategy should be individualized and keep in mind the ultimate goal to minimize exposure to long term antibiotics. Regardless, it should be noted that a patient will improve during any of these types of suppressive therapy, but once therapy is discontinued, the patient's risk of recurrent UTIs increases back to baseline. This again underscores the need for more effective long-term preventive strategies.

For those women who find sexual intercourse to commonly trigger an infection, post-coital therapy would be the easiest and safest option. Patient initiated therapy has been used for many years and is most beneficial for women who have infrequent or clustered recurrent UTIs. Adherent and motivated patients have been shown to be able to accurately self diagnose UTIs 95% of the time and successfully self treat with a short course of antibiotics taken at onset of symptoms [27]. Zhong et al found that patient-initiated single-dose intermittent antibiotic prophylaxis was as effective as low-dose daily antibiotic prophylaxis in the treatment of recurrent UTIs in post menopausal women and was associated with fewer gastrointestinal side effects [28].

Finally, continuous daily suppression has been shown in numerous studies to effectively reduce the incidence of recurrent UTIs by up to 95%. However, in an effort to decrease development of resistance, the first two options are recommended as initial therapy. This option should be reserved for those patients who don't respond to intermittent therapy or are unable to be compliant with it. Most clinicians treat for a 6 month period, but in patients who continue to have frequent episodes, longer periods varying from 2 to 5 years have been used.

The antibiotics most commonly used in suppressive therapies are nitrofurantoin, trimethoprim (TMP), trimethoprim with sulfamethoxazole (TMP/SMX), and fosfomycin. Quinolones or first generation cephalosporins were also used in some trials, but given their broader spectrum of action, they should NOT be used as prophylactic therapy. None of these antibiotics has shown superior effectiveness in UTI prophylaxis.

Nitrofurantoin is an attractive first choice as its bactericidal action is limited to the urinary tract. The dose most often used for prophylaxis is 50 to 100 mg/day, taken after intercourse or at bedtime with food. Once ingested, it has a very short half life in serum (about 30 minutes) and is excreted into the urine. It is effective against *Escherichia coli*, *Enterococcus*, *Staphylococcus aureus*, as well as some strains of *Klebsiella* and *Enterobacter*. Due to multiple sites of action, resistance has not been a problem despite over 55 years of use. Nitrofurantoin is not associated with impaired fertility or teratogenicity and is considered safe in pregnancy and breastfeeding. It has few drug interactions, making it an attractive choice for treating elderly patients on multiple medications. It should not be used in patients with impaired renal function. Primary side effects are nausea, emesis and anorexia [29].

Despite its overall safety, rare but serious adverse effects are reported. The most widely known is pulmonary toxicity [29]. Reports also exist of toxic hepatitis and blood dyscrasias [29]. Neurotoxicity from nitrofurantoin is less recognized, and is estimated to occur in 0.0007 percent of courses of therapy [29]. *All of these toxicities can be severe or even fatal, and their occurrence is independent of the length of time the drug is taken. Because these side effects are rare, practitioners who prescribe suppressive therapy with nitrofurantoin must be aware of these.*

Fosfomycin tromethamine is a powder mixed with four ounces of water and drunk. It is supplied in a sachet containing 3 grams. The dose is 3 gram as a one-time treatment of uncomplicated UTI. It has also been shown to be highly effective in prophylaxis of UTI recurrence at a dose of 3 grams every 10 days [30]. There is no data on its use as post-coital therapy. It inhibits bacterial cell wall synthesis and also decreases bacterial adherence of to the urothelium. It is most active against Staphylococci (including *S. Saprophiticus*) and *E. coli*, as well as some strains of *Pseudomonas* and *Proteus*. It is less active against enterococci, *Klebsiella spp*, *Enterobacter* and *Proteus mirabilis*. Good in vitro activity is reported against methicillin-resistant *S. aureus* (MRSA). It is Pregnancy Category B and is safe in pregnancy and breastfeeding. Side effects are mostly minor, including rash, nausea and diarrhea, headache, and back pain. There are rare reports in Drugdex of hepatic toxicity.

TMP-SMX has long been used as suppressive therapy and is effective. There is not much data on the effectiveness of Trimethoprim alone. The dose is trimethoprim 40 mg/sulfamethoxazole 200 mg either after intercourse, three times weekly, or daily. It is Pregnancy Category C but is considered safe to use in pregnancy, though if alternatives are available, another agent is recommended in the first trimester due to the folic acid antagonist activity of trimethoprim. It is also considered safe to use during breastfeeding. Increasing resistance to this agent should be noted. In the recent Antimicrobial Resistance Epidemiology in Females with Cystitis (ARSEC) study in nine European countries and Brazil, 30-50% of all isolated urinary pathogens were resistant to TMP-SMX [31]. Side effects of TMP-SMX are common and primary gastrointestinal: nausea, emesis and anorexia. Rash is also common. Rarely, more serious side effects occur such as Stevens-Johnson syndrome, toxic epidermal necrolysis or aplastic anemia.

3. Prevention of UTIS in the inpatient and institutional setting

UTIS are the most common nosocomial infection worldwide, accounting for about 40% of these. The great majority of these infections are due to the presence of an indwelling urethral catheter in hospitals and long-term care facilities (LTCF) and are commonly referred to as catheter-associated UTI (CAUTI). These infections add significantly to morbidity and sometimes even mortality for the patient. The cost of these infections is substantial, estimated at 2.66 billion dollars in 2007 US dollars [32].

More than 1.5 million people in the United States live in nursing homes. Within the last decade, the severity of illness of nursing home residents has increased such that these residents (average age 80) have a risk of developing health care-associated infection (HAI) that approaches that seen hospital inpatients. The use of indwelling foley catheters has decreased in this setting and is currently about 5 to 10%, but UTI remains the leading infection in long term care facilities (LTCFs). Guidelines for prevention of CA-UTI applies to both these settings [33]. Of note, the catheter literature commonly reports on catheter-associated asymptomatic bacteruria (CA-ASB) and catheter associated bacteruria if no distinction is made between CA-ASB and CA-UTI. CA-bacteruria is the predominant outcome measure reported in most clinical trials.

Undoubtedly, the best way to prevent UTI is to avoid long term catheterization. The risk of UTI goes up markedly about 72 hours after a foley catheter is inserted. As long term foley use is often unavoidable in the hospitalized or nursing home patient, much attention has been devoted to efforts to prevent CAUTI worldwide. The Department of Public Health in England developed guidelines in 2001 and updated them in 2007 [34]. A short time later, in 2008 the European Association of Urology (EAU), the Urological Association of Asia (UAA), and others published *European and Asian Guidelines on Management and Prevention of Catheter-Associated Urinary Tract* [35]. Within the United States, the Center for Disease Control (CDC) first published guidelines in 1981 and these have been intermittently revised, most recently in 2009 [36]. During this same year, the the Infectious Diseases Society of America published guidelines for the diagnosis, prevention and treatment of CAUTI as well [37].

Recently Conway and Larsen reviewed and compared a total of 8 guidelines worldwide to prevent CAUTI. They found broad agreement between the guidelines overall but noted that different grading systems for the level of evidence to support each recommendation made comparisons difficult. They also noted that most of the guidelines didn’t distinguish between true catheter associated infections as opposed to catheter associated asymptomatic bacteruria. They wisely noted that “For clinicians seeking to prevent CAUTI, the distinction is a moot point, because all symptomatic CAUTI begins as asymptomatic bacteruria”. Their article included an excellent, concise summary of all 8 of these guidelines. This included an overview of recommendations for catheter use, catheter types, insertion techniques, maintenance, and antimicrobials [38].

Within the United States, the guidelines for prevention are very similar between the CDC and ISDA 2009 guidelines. These guidelines are summarized below. The ISDA guidelines note that most of their recommendations pertain to the prevention of catheter-associated bacteruria as this is the reported outcome in most trials, whereas the CDC doesn’t differentiate between bacteruria and symptomatic UTI. Both guidelines provided evidence for strength of each recommendation. The CDC evidence levels were used in this summary and are defined in Table 1. They are noted in blue.

Category IA	A strong recommendation supported by high to moderate quality† evidence suggesting net clinical benefits or harms
Category IB	A strong recommendation supported by low quality evidence suggesting net clinical benefits or harms or an accepted practice (e.g., aseptic technique) supported by low to very low quality evidence
Category IC	A strong recommendation required by state or federal regulation.
Category II	A weak recommendation supported by any quality evidence suggesting a trade off between clinical benefits and harms
No recommendation/ unresolved issue	Unresolved issue for which there is low to very low quality evidence with uncertain trade offs between benefits and harms

Table 1. Modified HICPAC Categorization Scheme* for Recommendations (Reprinted from CDC [39]).

4. Recommendations for the prevention of CAUTI indications for use

- Insert catheter only for appropriate indications (see Table 2) and leave in place only as long as needed (Category 1B)

Catheters should NOT be placed for incontinence or nursing convenience. For the postoperative patient who needs an indwelling catheter, remove within 24 hours unless there are indications for continued use, such as surgery on the urinary tract or an open perineal wound. Then remember to remove as soon as medically feasible. The use of condom catheters in incontinent male patients should be considered but this is considered an unresolved issue due to insufficient data.

Patient has acute urinary retention or bladder outlet obstruction
Need for accurate measurements of urinary output in critically ill patients
Perioperative use for selected surgical procedures: 1. Patients undergoing urologic surgery or other surgery on contiguous structures of the genitourinary tract 2. Anticipated prolonged duration of surgery (catheters inserted for this reason should be removed in PACU) 3. Patients anticipated to receive large-volume infusions or diuretics during surgery 4. Need for intraoperative monitoring of urinary output
To assist in healing of open sacral or perineal wounds in incontinent patients
Patient requires prolonged immobilization (e.g., potentially unstable thoracic or lumbar spine, multiple traumatic injuries such as pelvic fractures)
To improve comfort for end of life care if needed
B. Examples of Inappropriate Uses of Indwelling Catheters
As a substitute for nursing care of the patient or resident with incontinence
As a means of obtaining urine for culture or other diagnostic tests when the patient can voluntarily void
For prolonged postoperative duration without appropriate indications (e.g., structural repair of urethra or contiguous structures, prolonged effect of epidural anaesthesia, etc.)

Table 2. Examples of Appropriate Indications for Indwelling Urethral Catheter Use (Reprinted from CDC [39]).

- Use alternative to indwelling catheters when appropriate
 - Condom catheters in male patients without obstruction or retention (Category II). The use of condom catheters vs indwelling catheter has been studied in a randomized controlled trial of hospitalized men aged 40 and over. Results showed condom catheter use is less likely to lead to bacteruria, symptomatic UTI, or death than the use of indwelling catheters. This was especially apparent in men without dementia, and the patients overwhelmingly preferred the condom catheters [40].
 - Intermittent catheterization for the following subgroups (Category II)

- Spinal cord injury patient
- Patients with bladder emptying dysfunction. This should include postoperative patients, including women with surgery on the genitourinary tract. Hakvoort et al randomized 87 patients who had recent vaginal prolapse surgery and a post void residual > 150 ccs after first void to either foley placement or clean intermittent catheterization (CIC). They found a significant decrease in bacteruria in the CIC group (12 vs 34%). The CIC patients also noted decreased time until return of spontaneous voiding: 18 hours in the CIC group versus 72 hours in the foley group [41]. Moreover, a subsequent study by this same group surveyed the study patients and found that the great majority preferred CIC instead of placement of a foley [42].
- Children with neurogenic badders, (e.g. myelomeningocele)
- Further research needed on (Unresolved issue)
- Benefits of urethral stent as an alternative to indwelling catheter in selected patients with bladder outlet obstruction
- Benefits of suprapubic catheters as an alternative to indwelling urethral catheters in patients requiring short or long term catheterization.

There are studies that have compared suprapubic catheters with urethral catheters. In the gynecology literature, there are few studies. A recent meta-analysis by Healy et al found only 12 randomized controlled trials. They found that although suprapubic catheters had lower overall infection rates when compared to urethral Foleys, (20% compared with 31%), the complication rates were higher (29 % vs 11%) [43]. One study randomized a group of 257 women who underwent anterior repairs with or without vaginal hysterectomy to 3 day suprapubic vs 3 day urethral foley vs 1 day urethral foley. There were fewer infections in the suprapubic group but a significantly higher risk of complications which led to early withdrawal of this arm of the study. Complications included blockage most commonly, urinary retention, and one pyelectasia. They authors concluded that in their trial, the optimal bladder catheter after anterior colporrhaphy was an urethral catheter for 24 hours [44]. Katsumi et al found that men with spinal cord injuries who need chronic catheterization have similar complication rates in terms of UTI, and recurrent bladder and renal calculi with urinary catheters as with suprapubic catheters. Catheter complications rates were similar, though differing in type. Men with urinary catheters had more urethral and scrotal complications, while men with suprapubic tubes had more leakage and 13% required revision [45].

5. Catheter insertion techniques

- Indwelling urethral catheters should be inserted with proper sterile technique and sterile equipment by trained personnel (Category IB)

- Use appropriate hand hygiene before and after insertion or any manipulation of catheter or site (Category 1B)
- Properly secure catheters after insertion to prevent movement and urethral trauma and traction (Category IB)
- Use a closed drainage system (Category IB)
- Use the smallest bore catheter possible to minimize trauma to the urethra and bladder neck (Category II)
- Intermittent catheter recommendations
 - Clean (non-sterile) technique is acceptable for patients requiring chronic intermittent catheterization (CIC) (Category IA)
 - Perform at regular intervals to prevent bladder overdistension (Category IB)
 - Optimal cleaning and storage methods for catheters used for CIC is not determined. (Unresolved issue)

6. Catheter maintenance techniques

- Maintenance of catheter once inserted (all Category IB)
 - Maintain closed drainage system
 - Keep urine flow unobstructed:
 - Avoid kinking
 - Keep collecting bag below level of bladder at all times
 - Empty the collecting bag regularly and avoid contact of the drainage spigot with the collecting container
- Changing of indwelling catheters or drainage bags at fixed intervals is not recommended. Change is only recommended for infection, obstruction or compromise of the system (Category II)
- Do **NOT** use systemic antibiotics routinely for the prevention of CAUTI in patients requiring either short or long term catheterization (Category IB)
 - Further research is needed on the prophylactic use of urinary antiseptics such as methenamine (unresolved issue).
- Do **NOT** use antiseptic solutions to clean the periurethral area while the catheter is in place. Routine hygiene (e.g., cleaning the meatal surface during daily bathing/showering) is appropriate (Category IB)

- Do **NOT** irrigate the catheter unless obstruction is anticipated, such as after prostate or bladder surgery where blood and debris is present within the system. If this is necessary, use closed continuous irrigation. (all Category II)
 - Routine irrigation of bladder with antibiotics is not recommended
 - Routine instillation of antiseptic or antimicrobial solutions into the urinary drainage bag is not recommended
 - Further research is needed on the use of bacterial interference (bladder inoculation with a nonpathogenic bacterial strain) to prevent UTI in patients requiring long term urinary catheterization (Unresolved issue)
- **Catheter materials:** there are antimicrobial catheters available that are coated with silver alloy or antibiotics and may reduce or delay the onset of bacteruria. This is an unresolved issue, but the CDC does recommend consideration of these catheters if the CAUTI rate is not decreasing in an institution despite the implementation of a comprehensive preventive strategy. (Category IB)
 - Silicone catheters might reduce the risk of encrustation in long-term catheterized patients with frequent obstruction (Category II)
 - Hydrophilic catheters, (catheters designed to be lubricated when moistened with water, which eases friction on the urethra upon insertion) might be preferable to standard catheters for patients using CIC (Category II)
 - The benefit of catheter valves in reducing the risk of CAUTI is unclear and further research is needed (unresolved issue). Catheter valves (see Figure 1) are small tubes usually 8 to 12 cm in length with a stopcock mechanism that fit on the end of a foley catheter, replacing the drainage bag. This allows the patient to self empty the catheter in a typical voiding fashion at regular intervals, doing away with the need for a drainage bag. They should not be used by patients with detrusor instability, as bladder wall contractions against a closed bladder outlet could lead to reflux. They also cannot be used by patients with cognitive impairment or limited manual dexterity



Figure 1. Colpoplast catheter valve

- **Management of obstruction: if this occurs and it is likely that the catheter material is contributing to obstruction, change the catheter (Category IB)**
 - Unresolved issues:
 - Benefit of irrigating catheter with acidifying solutions or use of oral urease inhibitors in patients with long-term indwelling catheters and frequent obstructions.
 - Use of portable bladder scanners to evaluate for obstruction in patients with indwelling catheters and low urine output
 - Use of methenamine to prevent encrustation in patients at high risk for obstruction
- **Specimen collection: (both Category IB)**
 - For culture: obtain these aseptically by aspirating the urine from the needleless sampling port with a sterile syringe after cleaning the port with disinfectant
 - Large volumes of urine for analysis (not culture) can be obtained aseptically from the drainage bag.

7. Quality Improvement (QI) programs

When implemented, there is good evidence that these programs can reduce the risk of CAUTI. (Category IB). Their purpose should be:

- To assure appropriate use of catheters
- To identify and remove catheters that are no longer needed: Alerts or reminders within the medical record that identify patients with catheters in place and note how many days they have been in have been shown to increase the removal rate of catheters. Even placing a sticker on the patient's chart reminding physicians to discontinue unnecessary foleys is beneficial. This simple intervention in a community hospital caused a significant reduction in the rate of CA-UTI after 3 months (7.02 vs 2.08; $P < .001$) and 6 months post-intervention (7.02 vs 2.72; $P < .001$) [46].
- To ensure adherence to hand hygiene and proper care of catheters.
- Guidelines for peri-operative catheter management:
 - Procedure specific guidelines for catheter placement preoperatively and post-operative removal
 - Protocols for management of postoperative urinary retention, such as nurse directed use of intermittent catheterization and use of ultrasound bladder scanners.

8. Other preventive measures

The use of prophylaxis for CAUTI with cranberry products is mentioned in the IDSA guidelines but not in the CDC, with the note that cranberry products should not be used routinely to reduce CAUTI in patients with neurogenic bladders with chronic intermittent OR indwelling catheters. They also noted insufficient data to recommend using cranberry products for other groups. However, these guidelines were published in 2009 before more recent studies that have shown some benefit to cranberry products. The previously cited study by Mutlu, although small, concluded that cranberry capsules could be an encouraging option for the prevention of recurrent UTI in children with neurogenic bladder caused by myelomeningocele who required chronic intermittent catheterization [47.] Because cranberry capsules are safe, inexpensive, well tolerated and don't cause any drug resistance, it would seem worthwhile to use them in these high risk populations as a first line preventive measures.

9. Conclusion

Urinary tract infection is one of the most common healthcare problems facing women, and almost half of women will have a UTI during their lifetime. The incidence is much lower in men, but increases with age. About 15% of women will have problems with recurrent UTI despite having no anatomic abnormalities of the urinary tract. This is likely due to genetic variations in their mucosal protective defense mechanisms that predispose them to bacterial colonization. Preventive strategies should be used liberally in this group of patients and should focus on non-pharmacologic measures first to avoid the ever-increasing drug resistance that is developing worldwide.

Simple hygienic measures are helpful, including proper wiping techniques and voiding after intercourse, and possibly avoiding tub baths. Diaphragms and contraceptive methods containing nonoxynol-9 should be avoided. Cranberry juice or tablets are likely an effective and risk free preventive measure, and should be taken three times daily. Methenamine is an old measure that has been shown to be effective for uncomplicated patients as well. After menopause, these women should use vaginal estrogen therapy which has been shown to decrease recurrences in several studies. If patients continue to have frequent infections despite these measures, a regimen of antibiotic prophylaxis should be started. This can be a single dose taken after intercourse if the patient is sexually active and intercourse triggers an infection. For women who don't have this problem but still have frequent infections, patient-initiated therapy is very effective. The patient has a supply of antibiotic on hand to take at the first sign of symptoms. Finally, for women who continue to have infections despite these strategies, a daily dose of suppression may be needed for 3 to 6 months. However, her risk of infection returns to baseline and remains high when this therapy is discontinued. The antibiotics used most often in suppressive regimens are nitrofurantoin and TMP/SMX

CAUTI remains the leading cause of hospital acquired infections worldwide. Although use of a urethral catheter is at times a necessary part of caring for patients, there are proven steps that

can decrease the infection rate. Most importantly, catheters should be placed only for accepted indications and not for incontinence or convenience. For postoperative female patients undergoing uncomplicated procedures, including gynecologic procedures, we should rethink the practice of routine foley placement during the procedure. Instead, consider intermittent in/out catheterization until she is able to ambulate and void satisfactorily. For men without cognitive impairment and obstruction, a condom catheter should be used. More research is needed in the bladder management of the postoperative patient, as well as the role of cranberry to prevent CAUTI. When Foleys are placed, the need for ongoing catheterization should be assessed daily and the catheter discontinued as soon as possible. Reminder systems, whether an electronic reminder or a paper sticker for those not yet using electronic systems, have been shown to lower infection rates and should always be used when a foley is placed.

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