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Urinary Tract Infections in Women: Pathogenesis, Diagnosis, and Management

Justin T. Matulay[1] · **Carrie M. Mlynarczyk**[1] · **Kimberly L. Cooper**[1]

Abstract Urinary tract infections (UTIs) in women represent one of the most common disease entities in both the ambulatory and hospital setting. Nearly 60 % of all women will experience at least one UTI in their lifetime leading to billions of dollars of healthcare spending. There are several important factors on both a pathogen and host level that support bacterial colonization with ultimate progression to infection in otherwise healthy patients. In an era of increasing healthcare costs and limited face-to-face evaluation time, establishing the correct diagnosis can prove challenging and leads to misguided and sometimes excessive treatment. Ultimately, a stronger focus on preventative strategies may help to reduce the impact of uncomplicated UTIs on women.

Keywords Urinary tract infection · Bacteriuria · Antibiotic use in UTIs

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✉ Kimberly L. Cooper
klc11@cumc.columbia.edu

Justin T. Matulay
jtm2141@cumc.columbia.edu

Carrie M. Mlynarczyk
cmm2236@cumc.columbia.edu

1 Department of Urology, Columbia University Medical Center, 161 Fort Washington Ave 11th Floor, New York, NY 10032, USA

Introduction

Epidemiology

Urinary tract infection (UTI) represents a common disease entity among women with 50 to 60 % experiencing at least one during their lifetime [1, 2]. This places a significant burden on the healthcare system as UTI symptoms accounted for approximately 10.5 million ambulatory visits in the USA in 2007, of which nearly 3 million took place in an emergency department and 1 million led to hospital admission [3]. Nearly 25 % of women report recurrent infection within 6 months after first diagnosis and as many as 12 % report experiencing at least one UTI per year [4]. The cost of evaluation and treatment of UTIs is in the vicinity of $3.5 billion annually [3, 5]. Beyond the economical impact, there is also concern regarding widespread use of antibiotics, the necessary dose and duration of which are often overestimated leading to microbial resistance.

Definitions (Table 1)

The presence of bacteria in the urine, known as bacteriuria, may be indicative of infection or colonization of the urinary tract, but it may also be due to bacterial contamination occurring during collection of a specimen [6]. Bacteriuria does not always occur in conjunction with symptoms (*asymptomatic bacteriuria*), but when it does (*symptomatic bacteriuria*), this typically represents urothelial inflammation due to urinary tract infection. The clinical syndrome of *cystitis* is defined by the presence of lower urinary tract symptoms such as frequency, urgency, and/or dysuria. *Acute pyelonephritis*, another clinical syndrome, is characterized by fever, chills, and flank pain. Broadly speaking, UTIs are clinically divided into two main categories, uncomplicated and complicated. An uncomplicated

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Table 1 Definitions

Uncomplicated vs. Complicated	
Uncomplicated	Healthy, non-pregnant woman
Complicated	Men, structural abnormality (obstruction, diverticulum, prior urologic surgery), neurologic impairment (dementia, multiple sclerosis), diabetes, immunocompromise, foreign body (calculus, urologic instrumentation, urinary catheter), pregnancy, recent antimicrobial use
Anatomic Location	
Bacteriuria	Presence of bacteria in urine specimen detected on urine culture; the threshold above which infection is indicated varies based on collection method (suprapubic aspiration, urethral catheterization, voided); can be asymptomatic or symptomatic
Cystitis	Clinical syndrome of frequency, urgency, dysuria, and/or suprapubic pain; usually due to bacterial infection of the bladder but symptoms may also be related to urethritis, vaginitis, or interstitial cystitis
Pyelonephritis	Clinical syndrome of fever, chills, and flank pain; bacterial infection of the kidney

UTI is defined as one occurring in an otherwise healthy, non-pregnant woman with a structurally and neurologically normal urinary tract. All other UTIs are considered complicated and include those occurring in the presence of a foreign body, such as catheters or calculi, or in patients with impaired urinary tract structure or function, as is the case with urinary obstruction, pregnancy, or retention due to neurologic impairment [3, 7].

Pathogenesis

Humans are normally able to clear foreign organisms from the urinary tract through regular voiding, immune system response, and antimicrobial factors in the urine, but some pathogens have developed mechanisms to evade such defenses and successfully establish infection.

Microbiology

Infection of the urinary tract is caused primarily by both gram-negative and gram-positive bacteria, usually facultative anaerobes of the bowel flora, but skin and vaginal flora can also be pathogenic [6]. Certain types of fungi, parasites, and, less commonly in recent times, mycobacteria, are also known to cause UTIs. The most common organism isolated from urine culture in patients with a UTI, whether complicated or uncomplicated, is uropathogenic *Escherichia coli* (UPEC) accounting for 70–80 % of community-acquired infections and 40–60 % of healthcare-associated infections [8–11]. Other common isolates include *Klebsiella* spp., *Staphylococcus saprophyticus*, Group B *Streptococcus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and Candida spp., though the precise frequency of these "second-tier" organisms varies based on the patient population. For example, *S. saprophyticus* causes 10 % of UTIs in young, sexually active females whereas it is rarely seen in the elderly or males. In a retrospective review of 40,618 episodes of UTI, Laupland et al. [10] found that 84.2 % of *S. saprophyticus* isolates came from females between 10 and 49 years old. Meanwhile, *Enterococcus* spp. are responsible for 11.6 % of nursing home UTIs compared to 5.3 % in the community. Although gram positives are often isolated in urine cultures, it is controversial whether their mere presence should trigger treatment. It must be kept in mind that gram positives are often contaminants, and the decision of whether to treat with antibiotics should take into consideration the results of the urinalysis in conjunction with culture results.

The ascending route is responsible for introduction of pathogenic organisms into the urinary tract in nearly all cases of uncomplicated UTI. Adherence of pathogens to the urothelial surface of the urethra allows for migration into the bladder where infection can be established. Bacteria causing uncomplicated UTIs, such as UPEC and *K. pneumoniae*, are capable of directly binding the superficial bladder epithelium via receptors expressed on the surface of umbrella cells known as uroplakins [3, 12]. The most commonly studied uropathogen, UPEC, contains type 1 pili on its cell surface. This mannose-containing receptor, variations of which can be found on most family members of the *Enterobacteriaceae* family, is able to recognize and bind tightly to uroplakins found mainly in the lower tract, setting the stage for cell entry [13]. In contrast, P-fimbriae expression is associated with bacterial adhesion within the upper tract, and it is also believed that dissemination beyond the bladder may require flagellum-mediated motility to ascend against the flow of urine [14].

Rapid proliferation occurs within the host cell but several toxins released by the invading bacteria cause destruction of the urothelium, providing greater access to nutrients and promoting deeper penetration while at the same time creating a proinflammatory environment [12]. The immune system is typically able to kill *E. coli* via the complement system and/or natural killer (NK) cell phagocytosis but UPEC have evolved evasive mechanisms to circumvent these measures. For example, the O-antigen of lipopolysaccharide (LPS), a highly immunogenic compound found in the cell wall of most gram-negative bacteria, acts as both a toxin and immunoprotectant with each of the various serotypes responsible for bacterial persistence in different anatomical locations [15, 16].

Host Factors

Women account for approximately 85 % of all UTIs diagnosed annually representing a nearly sixfold increased risk compared to men for all age groups, with the exception of infancy (<1 year old) [10, 17]. One prominent reason for a gender difference in UTIs is the anatomy of the female genitalia and urinary tract. First, the urethral meatus is located within the vaginal introitus and is in close proximity to the anus, both of which can serve as sources of external bacteria, especially when manipulation occurs, as with sexual activity, catheter insertion, and toileting habits. Second, once bacteria have gained entry to the urethra, there is a much shorter length to travel between the meatus and bladder neck in women when compared to men.

The presence of bacteria within the urine does not constitute infection and, as mentioned earlier, regular voiding helps to clear transient bacteriuria. However, persistence of urine in the bladder due to urologic conditions that impair voiding increases the likelihood of infection. Normal vaginal flora consisting of lactobacilli, coagulase-negative staphylococci, streptococci, and corynebacteria form a microenvironment that is inhibitory to uropathogenic strains of bacteria, but use of spermicides alters the flora and predisposes to UTI. Diaphragm use has been identified as a risk factor due to obstruction of urine flow and/or concomitant spermicide use [2, 17, 18]. Menopause also confers an increased risk in women due to decreased levels of estrogen. Estrogen in the vaginal canal helps maintain an acidic environment that is more hostile to uropathogenic bacteria. Pregnancy poses an increased UTI risk because of associated physiologic (e.g., decreased ureteral peristalsis) and anatomic (e.g., ureteral obstruction by gravid uterus) changes of the urinary tract [19, 20]. Type 2 diabetes has been shown to increase UTI risk by 1.5–2-fold over non-diabetics, and though the exact mechanism has yet to be uncovered, there are several potential explanations including glycosuria, immunosuppression, and voiding dysfunction [21–23]. Genetic differences have been identified in toll-like receptor 4 and CXC chemokine receptor 1 that are associated with impaired host immune response, and some individuals show increased expression of cell surface receptors for bacterial fimbriae [24•, 25]. In fact, family history of UTIs is a known risk factor in women, which supports the notion that genetics play a crucial role in determining which women are more susceptible to developing UTIs. Additionally, recent use of antimicrobials confers an increased risk of developing a UTI, perhaps because the normal flora levels are diminished and allow for opportunistic uropathogens to flourish.

Diagnosis

History and Physical Examination

The diagnosis of UTI is commonly made by using a combination of symptoms with a positive laboratory test [26]. Information from the history can help determine the likelihood of a UTI including history of UTIs and recent sexual activity. Presenting symptoms of urinary tract infections commonly include dysuria, frequency, urgency, suprapubic pain, and hematuria. Upper tract symptoms seen in pyelonephritis include fever, chills, and flank pain. Meister et al. [27] completed a systematic review to evaluate the role of history and physical exam in diagnosing UTIs and found no single history or physical exam finding could independently predict UTI. A meta-analysis by Bent et al. [28] found that dysuria, frequency, hematuria, and back pain significantly increased the probability of a UTI. Women presenting in the outpatient setting with two out of three symptoms of dysuria, urgency, or frequency and without vaginal discharge had greater than a 90 % chance of having a UTI. Therefore, a focused history and physical exam is reliable for the diagnosis of uncomplicated UTI in most cases.

Conversely, a positive laboratory finding in the absence of symptoms is considered asymptomatic bacteriuria and does not require treatment. This cannot be overstated enough, as treatment of asymptomatic bacteriuria contributes to significant overuse of unnecessary antibiotics. In 2005, the Infectious Disease Society of America (IDSA) published guidelines for management of asymptomatic bacteriuria [29]. These guidelines recommend against screening for or treating asymptomatic bacteriuria in healthy non-pregnant women. Unfortunately, these guidelines are often ignored, and women with a positive urine culture, in the absence of symptoms, are mistakenly diagnosed with a UTI and started on antibiotics.

Laboratory Studies

Laboratory studies for the diagnosis of UTI include urine dipstick testing, microscopic urinalysis, and urine culture. Given that there is a high pretest probability of UTI based on symptoms alone, there is no need for confirmatory urine testing in an initial uncomplicated UTI [30]. This approach is not recommended in all patient populations, however, as those with recurrent UTIs, complicated UTIs, or a history of multi-drug-resistant organisms should have a urine culture sent prior to initiation of therapy [31].

The manner in which a urine specimen for culture is collected holds significance in the interpretation of the results. Urine can be collected as a clean catch, a catheterized specimen, or from suprapubic aspiration. When using a clean catch method, contamination from urethral or vaginal flora is a common problem that may complicate the diagnostic accuracy of such a specimen [26]. Indeed, body habitus, atrophic vaginal mucosa, and manual dexterity can preclude the acquisition of a good clean catch sample. In a recent study conducted by Hooton et al. [32•], midstream clean catch specimens were compared to catheterized specimens in a cohort of premenopausal women. They found that *E. coli* on a clean catch was strongly correlated with growth from a catheterized specimen, as were findings of *K. pneumonia* and *Staphylococcus*, while *Enterococcus* and group B *streptococci* were likely to represent contamination. Furthermore, even at low colony counts ($\geq 10^2$ cfu/mL), *E. coli* has good positive predictive value of 93 % and increases to 99 % when using a threshold of $\geq 10^4$ cfu/mL. The diagnosis for urinary tract infection was historically defined as the finding of greater than 10^5 colony-forming units (CFUs) of bacteria in a urinary culture [28, 33]. However, further studies have shown that women with cultures with lower CFUs in midstream specimens can have similar clinical presentations [33]. Bacteria levels can be decreased with frequent emptying associated with the dysuria and irritation often seen in UTIs. Furthermore, a bacterial level of 10^5 CFU can be found from contamination in women with large numbers of pathogenic bacteria on the perineum, which is often found in women susceptible to infection [26].

Urinalysis is a screening tool for UTI that uses markers of infection to detect the presence of pathogenic bacteria and has long been relied upon for its ease of use and widespread availability [33]. According to one study, a positive leukocyte esterase reaction offers superior sensitivity compared to nitrite positivity (84 % vs. 44 %) but falls short in specificity (59 % vs. 97 %). There are several published sources on this topic, but exact values are difficult to obtain due to the widely varied collection techniques and healthcare settings in the published literature on the topic [34].

In order to make an accurate diagnosis of UTI, results from a urine culture (obtained in a proper manner) should be analyzed in conjunction with results of a urinalysis and should be considered in the context of the presence or absence of urinary symptoms. If a culture is positive but the urinalysis is negative, and symptoms are vague, a catheterized sample should be obtained. In many cases, a catheterized sample will be negative under these circumstances, and unnecessary antibiotic use will be avoided.

Imaging/Cystoscopy

Imaging studies are generally not needed for uncomplicated UTIs. Renal ultrasound can be useful to assess for post void residual particularly in older females with recurrent UTIs, but cystoscopy should only be used if an abnormality is found. CT and intravenous urography can be used for patients with abnormal ultrasound findings or if there is a concern for abscesses. Other patients that may benefit from CT include patients with diabetes or neurogenic bladders [26]. In cases of pyelonephritis, the EAU recommends obtaining upper tract imaging to rule-out obstruction as UTI may rapidly progress to urosepsis under these conditions if not decompressed promptly [35].

Treatment

Most uncomplicated UTIs can be successfully treated with a short course of empiric antibiotic therapy targeted at UPEC. The IDSA published its most recent guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in pre-menopausal non-pregnant women in 2011 based on an extensive literature review conducted by an expert panel [36•]. Their recommendations take into account several factors including most efficacious agents, potential for regional variability in resistance patterns, and potential for "collateral damage" to the host microbiome. For acute uncomplicated cystitis, the ISDA panel recommends four potential empirical first line agents: (1) nitrofurantoin monohydrate/macrocrystals 100 mg twice daily for 5 days, (2) trimethoprim-sulfamethoxazole (TMP-SMX) 160/800 mg twice daily for 3 days, (3) fosfomycin trometamol 3 g as a single dose, and (4) pivmecillinam 400 mg twice daily for 5 days. Individual patient factors such as allergy history, availability, and tolerance should be considered when prescribing. If none of these agents can be used, then the second line choice is between a fluoroquinolone for 3 days or β-lactam (including amoxicillin-clavulanate, cefdinir, cefaclor, cefpodoxime-proxetil) for 3 to 7 days. In the USA, pivmecillinam is not available, and fosfomycin is very expensive, so these are generally not used as first-line agents. However, fosfomycin is an excellent choice of treatment for outpatient management of multi-drug-resistant *E coli*.

The use of nitrofurantoin has increased since the latter part of the last decade when several guidelines in the US and Europe recommended its use as a first-line agent when being faced with increasing bacterial resistance to fluroquinolones and β-lactams. Nitrofurantoin is cleared quickly by the kidneys and concentrates in the urinary tract where its exact mechanism of bacterial killing is unknown. Blood levels are usually undetectable (except in severe end-stage renal disease) making it a safe agent with minimal side effects. A recent meta-analysis found toxicity—limited to nausea, abdominal discomfort, and headaches—to be reported at 5 to 16 % in patients treated with short-course therapy (<7 days) [37]. Clinical cure was reported in 79 to 92 % and microbiological cure in 80 to 92 % of patients included in the analysis giving nitrofurantoin similar efficacy to TMP-SMX, fluroquinolones, amoxicillin, and fosfomycin. The lack of detectable blood levels of nitrofurantoin means that it is considered an ineffective agent against pyelonephritis and should be avoided in those patients. It should be mentioned that adverse effects of long-term treatment can be significant, including pulmonary fibrosis and/or diffuse interstitial pneumonitis as well as renal and neurologic toxicity. Additionally, this medication must be used with caution in the elderly [38].

Acute uncomplicated pyelonephritis that is not severe enough to warrant hospitalization can be managed adequately with empiric oral antibiotics according to the following IDSA guideline recommendations: (1) ciprofloxacin 500 mg twice daily for 7 days, (2) levofloxacin 750 mg daily for 5 days, (3) TMP-SMX 160/800 mg daily for 14 days, and (4) β-lactam agent for 10–14 days following initial administration of a long-acting IV antibiotic (ceftriaxone or an aminoglycoside) [36•]. As with acute uncomplicated cystitis, community-specific resistance patterns should inform antibiotic choice, and an agent with <10 % resistance is preferred.

Women who have had previous UTIs may be candidates for patient-initiated therapy based on self-diagnosis of acute uncomplicated cystitis [31]. Patients are given a prescription for a standard empiric antibiotic regimen and instructed to begin therapy with symptomatic onset. The success of this approach relies on a well-established physician-patient relationship and education of symptoms that should prompt a visit to the physician's office or emergency department. Previous studies have shown that patients can accurately diagnose their UTI in >90 % of cases while reporting superior satisfaction rates compared to traditional care [39, 40]. There has been some interest in delayed antibiotic treatment and/or symptomatic treatment with NSAIDs but the evidence shows such a high proportion of patients ultimately receiving definitive antibiotics that immediate therapy remains the best management option [30, 31, 41, 42]. However, self-start therapy is not always the best option and may lead to significant overtreatment. In our practice, we support this as an option but insist that patients provide samples prior to initiating therapy.

As mentioned earlier, treatment of asymptomatic bacteriuria is currently not recommended in otherwise healthy non-pregnant women due to the risks associated with antibiotic overtreatment, both for the individual patient and the population as a whole. Positive urine cultures in the absence of symptoms are likely to reflect colonization rather than infection, and there is currently no known negative effect. In a study of 490 women followed for a mean of 12 years having asymptomatic bacteriuria had no impact on renal function, and, despite another analysis of essentially the same patients finding an increased risk of hypertension, the group with asymptomatic bacteriuria had higher blood pressure at baseline so it is difficult to draw a conclusion based on this data [43, 44]. Trautner and Grigoryan identified five groups of women in whom asymptomatic bacteriuria should not be treated (Fig. 1).

In the past, asymptomatic bacteriuria was considered a risk factor for the development of recurrent UTIs. However, recent data suggests the opposite. In fact, current thinking is that treatment may eradicate the protective benefit of some asymptomatic strains. A study by Cai et al. [46] looked at women with recurrent UTIs who presented to an Italian STD clinic. They found that at 6 months, 7.6 % of women not treated developed a UTI while 29.7 % of those treated for asymptomatic bacteriuria became symptomatic and were treated for a UTI.

Prevention

As previously mentioned, the prevalence of UTI in women places it among the most common ailments encountered in medical practice, especially in the ambulatory setting, and as such, efforts should be focused not only on proper antibiotic treatment but also on preventing recurrence as a way to help limit the widespread use of antibiotics.

Behavioral Modification

Women who use contraceptive techniques known to be associated with recurrent UTIs, such as diaphragm and/or spermicide use, should be counseled on the risks and benefits of switching to an alternative form of birth control. Investigators have tried, but thus far failed, to identify other behavioral trends that lead to an increased risk of developing a UTI, including post-coital voiding, wiping habits, and avoidance of douches [5, 18, 47, 48]. Patients may choose to adopt techniques based on anecdotal evidence but should be made aware that there is no scientific evidence to support any change in behavior.

Antibiotic Prophylaxis

The use of low-dose continuous antibiotics is one option for preventing recurrent UTIs. Studies have evaluated the efficacy of several medications for this purpose, and the most common regimens are nitrofurantoin 50–100 mg daily, TMP-SMX 40 mg/200 mg daily, cephalexin 125–250 mg daily, ciprofloxacin 125 mg daily, or fosfomycin 3 g every 10 days [49•, 50–52]. Continuous antibiotic prophylaxis was determined to be significantly better than placebo for prevention of recurrent UTI in women in a 2004 Cochrane review; however, changes in antimicrobial resistance during the intervening

1. Non-pregnant
2. Diabetics
3. Elderly living in the community
4. Spinal cord injury patients
5. Catheterized patients while the catheter is in place

Fig. 1 Populations of women who should not be treated for asymptomatic bacteriuria [45] decade calls into question the modern day applicability of this result [53]. Additionally, once antibiotic prophylaxis is discontinued, the risk of recurrent UTIs remains the same; therefore, there does not appear to be a long-term benefit. What is clear is that there is great risk associated with daily antibiotic use, to individuals as well as society overall, due to adverse effects and increased resistance patterns. A more recent systematic review by Eells et al. [50] compared daily nitrofurantoin prophylaxis to four non-antibiotic regimens and found the former to be the most efficacious and cost-effective. Yet, the conclusions of this study emphasized that finding options other than daily nitrofurantoin use is preferable. Post-coital prophylaxis reduces the overall dosage of antimicrobials administered while maintaining efficacy. In one randomized trial, post-coital ciprofloxacin had the same effect as daily ciprofloxacin prophylaxis over the course of 1 year for sexually active young women [54].

Cranberry Products

Much has been written on the use of cranberries in UTI prophylaxis both in scientific and lay publications. It is an appealing option to many women because of its status as a "natural" remedy rather than a pharmaceutical agent. A recent Cochrane review examined 24 studies comparing cranberry products to placebo and/or antibiotic prophylaxis but the results were difficult to interpret based on the heterogeneity of both the particular product used and the available literature [55•]. One of the main problems lies in the lack of uniformity in reporting the content of proanthocyanidins (PACs), the active ingredient, in various cranberry preparations. Furthermore, many women find cranberry products unpalatable, and dropout is typically high; however, side effects are minimal, and some studies have demonstrated beneficial effects [51, 56–58]. For women who are able to tolerate cranberry products, a dose of 36 mg of PAC may reduce the risk of recurrent UTIs but the lack of standardization and regulation in the marketplace makes it difficult to select an appropriate product [59].

Methenamine

Methenamine is an oral drug that is 70–90 % renally excreted and converted to formaldehyde and ammonia in an acidic environment (pH<6), with the former compound exhibiting nonspecific antibacterial activity [60]. One preparation of the compound, methenamine hippurate, has been tested in several studies, including two randomized placebo-controlled trials conducted in otherwise healthy women showing a 56 to 75 % reduction in recurrent UTIs, but has received little attention more recently [61, 62]. A Cochrane review of the available evidence concluded that there was significant heterogeneity in available studies so a strong conclusion could not be made; however, there may be a benefit to short-term (≤7 days) therapy in non-neurogenic patients without an indwelling catheter [63]. While the literature in support of methenamine use may not be abundant, in our practice methenamine is preferable to the use of daily antibiotic prophylaxis since it does not contribute to overall increase in resistance and is generally well-tolerated.

Estrogen

The female urethra and distal vagina are embryologically linked and exhibit similar hormonal sensitivity. The normally acidic microenvironment of the vaginal epithelium is supported by estrogen and helps to inhibit bacterial overgrowth with enteric organisms while also improving anatomic contributors to recurrent UTIs, such as prolapse [64, 65•]. In postmenopausal women, local application of vaginal estrogen has been proven effective at preventing recurrent UTIs while systemic therapy has not [66].

Future Directions

Vaccination with heat-killed uropathogenic strains of *E. coli* offers an alternative to antibiotic prophylaxis, and early evidence seems to support its use. In a meta-analysis of 891 patients, Beerepoot et al. [65•] found that the oral vaccine OM-89 (Uro-Vaxom®) reduced the mean number of UTIs by half. A vaginal vaccine (Urovac) was also analyzed but showed only a mild reduction in recurrent UTIs and was associated with vaginal irritation in nearly 28 % of patients. As mentioned earlier, D-mannose is a naturally occurring compound expressed by urothelial cells and facilitates bacterial attachment via type 1 fimbriae [67]. When administered orally in supraphysiologic concentrations (1 g daily), it is excreted in the urine and saturates type 1 fimbriae binding sites. A randomized, placebo-controlled study showed similar efficacy between nitrofurantoin and D-mannose at preventing UTIs when compared to placebo in otherwise healthy women [68]. The use of probiotics is a familiar concept in for gastrointestinal disorders but can also be applied to the urinary tract. Application of lactobacilli via vaginal suppository showed initial promise in one study, reducing the risk of recurrence when compared to placebo, but did not fare as well against TMP-SMX prophylaxis in a subsequent trial [69, 70].

Conclusions

UTIs impact women at an individual level but also hold societal significance. The relatively high annual incidence translates into billions of healthcare dollars spent on diagnosis and treatment, not to mention any related reduction in workforce productivity. At a time when providers are faced with pressure to see more patients in less time, there is an impulse to treat with empiric antibiotics, though evidence suggests that it will become increasingly more difficult to find an effective agent. As 20 to 30 % of UTIs are recurrences, it is important to consider alternative strategies in UTI management. Patient-directed therapy has been shown to improve patient satisfaction rates and can be highly effective in selected patient populations. Continuous antibiotic prophylaxis may be effective in the short-term; however, it is not without significant risk. Several non-antimicrobial agents have been tested with varying degrees of success but will require further investigation before firm recommendations can be made.

Compliance With Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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