Updates in the Diagnosis & Management of Female Urinary Tract Infections

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ABSTRACT

Urinary tract infections are considered one of the most common bacterial infections among adult women. Acute uncomplicated cystitis can be identified by the presence of symptoms along with positive urinalysis result. Urine culture is not always required to diagnose urinary tract infections. The guidelines recommend the use of fosfomycin, nitrofurantoin, or trimethoprim-sulfamethoxazole as first line agents targeting the gram negative pathogens which are the causative organisms in most of the cases. However, the wide use of antibiotics has led to the development of multi-drug resistant pathogens. Researchers and clinicians are studying the new diagnostic techniques and the use of antibiotic sparing methods for the management of UTI, to reduce the occurrence of resistant organisms.

Keywords: Urinary tract infection, Classification, Risk factors, Clinical presentation, Diagnosis, Current treatment options, New antibiotics
INTRODUCTION

Urinary tract infection (UTI) is the most common bacterial infection worldwide, in which 35% of healthy women suffer from symptoms of urinary tract infection at some point in their lifetime. It is considered to be the most common bacterial infection in the United States reaching almost 8 million outpatient clinic visits and 1 million emergency visits each year, resulting in approximately 100,000 hospitalizations [1,2]. The incidence of UTIs varies, due to lack of report in most of the areas [3]. UTI is the infection that affects any part of the urinary system. When it affects the lower tract, it is known as acute cystitis, and when it affects the upper tract, it is known as acute pyelonephritis [4,5].

Risk Factors

Risk factors of recurrent symptomatic UTI include diabetes, multiple sclerosis, older age, pregnancy state, functional disability, patients with spinal cord injuries or catheter use, patients with acquired immunodeficiency syndrome, urinary retention or incontinence, recent sexual intercourse and history of urogynecologic surgery [1].

Classifications

UTI is classified according to the symptoms and host characteristics. It can be an acute (uncomplicated), recurrent, or complicated [6,7]. UTI in clinical practice has a broad range of presentation. It ranges from an asymptomatic bacteriuria, or symptomatic and recurrent UTIs, or sepsis associated with UTI requiring hospitalization [8].

Uncomplicated symptomatic UTIs are considered in a healthy genitourinary tract with no prior instrumentation. The presence of UTI is approached when there is a symptomatic infection of the bladder revealed by fever, aggravated urinary frequency or urgency, dysuria, suprapubic tenderness, costovertebral angle pain or tenderness with no apparent cause, and laboratory tests showing UTI. In older women with symptomatic UTI localized to the bladder, fever may not always present [9].

Complicated UTI is recognized in patients with symptomatic UTI caused by a structural or functional abnormality; who had urinary instrumentation; systemic diseases such as renal insufficiency, diabetes, or immunodeficiency; or who undergone organ transplantation [10-13].

Pyuria defined as the presence of leukocytes in the urine. Specifically, the presence of 6-10 or more neutrophils per high power field of unspun, voided mid-stream urine [14].

Recurrent UTI is defined by the presence of two or more infections in six months or three or more in one year period. There is evidence suggests that recurrent UTIs could have a genetic component [15-17]. Diabetes is considered a significant risk factor for recurrent UTIs in women [18,19]. Recurrent UTIs with similar or different uropathogens are commonly seen in outpatients, leading to frequent outpatient visits and increased number of prophylactic or therapeutic antibiotic use, anxiety, and low morale [20,21].
DIAGNOSIS

Establishing a diagnosis of symptomatic UTI in women is very crucial. It requires careful clinical evaluation for the presence of systematic or localized symptoms and a laboratory testing using urine culture. In acute, outpatient settings, the lack of urine culture makes the diagnosis more challenging. The presence of two out of three (dysuria, frequency, or urgency) in women is highly predictable for the diagnosis of acute cystitis [22]. This high probability will not be improved by adding a urinary dipstick testing looking for leukocyte esterase. Randomized trials found that the addition of urine dipstick testing or urine culture was not associated with better outcomes than empiric therapy in terms of symptoms relief or time to consultation [23]. Accordingly, in the presence of clear symptoms, an outpatient visit without urinary testing is an acceptable strategy to manage acute cystitis. Women with relapse or recurrent infections, women with complicated infection, or those in whom multidrug-resistant organisms are suspected based on previous microbiology or exposure to antimicrobials should have a urine culture performed. Catheter-associated UTI is the most common nosocomial infection, reaching more than 1 million cases in hospitals and home nursing [24]. The risk of UTI increases with a prolonged duration of catheterization. This risk is increased with the high prevalence of chronic genitourinary symptoms, low cognition and a high comorbidity load with old age, diagnosis, and management of symptomatic UTI remains a challenge among elderlies (Figure 1). In these patients, acute dysuria is more discriminating for UTI than other genitourinary symptoms [8]. It is crucial for the health caregiver to be aware to recognize asymptomatic bacteriuria from symptomatic UTI. Senior women with asymptomatic bacteriuria should not be treated [25].
Figure 1: Options for Uncomplicated UTI in Out-Patient Source: JAMA. 2014; 311(8):844-854.

Urinary Testing

The urinary dipstick, although very simple and convenient, has variable test characteristics [26]. Urine dipstick sensitivity and specificity for leukocyte esterase, nitrites, or both vary among different patients. The sensitivity and specificity for a positive dipstick test in patients with UTI was 82% and 71%, respectively [27]. The negative predictive value for dipstick testing of other studies from varies 92% to 100% [4, 22]. Urine dipstick analysis should be performed in the outpatient setting to reach a diagnosis of UTI. In a low pretest probability of UTI and negative leukocyte esterase and nitrites in urine dipstick, it excludes the presence of infection and eliminates the
need to obtain urinalysis and urine culture. Limitation of dipstick testing effectiveness comes with high false-positive rates [27].

Further urinary studies are conducted for patients with UTI with high pretest probability. The presence of pyuria is confirmed by a laboratory-based clean-catch urinalysis if there at least ten WBCs in a high-powered field and positive urine culture of not less than 105 CFU/mL of an identified organism and the uropathogen [8].

In outpatient clinics, the patients themselves should collect a clean-catch urine sample. While female patients, need to separate their labia and clean the urethral area with an antiseptic soap solution starting from front to back before voiding. The initial urinary flow should be discarded, then collect the midstream urine into a sterile container. A simple voided urine can be used, although less efficient, If a clean-catch urine specimen is challenging for a patient to obtain (e.g., obesity, arthritis) [4].

**Urine Culture**

The optimal diagnosis of UTI include both clinical signs/symptoms and laboratory evidence of a urinary infection (bacteriurea ≥ 10,000 CFU/mL & pyuria 10 WBC/high-power field). If other causes cannot identify, patients presenting with any 2 of the following meet the clinical diagnostic criteria for symptomatic UTI: fever, acute dysuria, worsened urinary urgency or frequency, supra pubic tenderness, or costovertebral angle pain or tenderness [8]. An infection can be excluded in a negative dipstick result for leukocyte esterase and nitrites in a low pretest probability of UTI. Urine dipsticks may lead to false-negative in cases of non-nitrite-producing pathogens, such as Enterococcus and Staphylococcus spp., or in diluted urine samples [22]. A positive urine culture (≥10,000 CFU/mL) with no more than two uropathogens and pyuria confirm the diagnosis of UTI. It is of high importance to determine the antimicrobial susceptibility when managing UTI. Urine dipstick can help in the diagnosis of UTI but it cannot identify the exact uropathogen nor the antimicrobial susceptibility. Urine culture and sensitivity remain the gold standard approach. It requires a clinical laboratory setting and it takes 2-3 days to get the final result. The emergence of drug-resistant and multidrug-resistant pathogens has further complicated the usual treatment of urinary tract infections [28].

**New Diagnostic Technologies**

New diagnostic tools, such as mass spectrometry and nucleic acid tests, show improvement in the speed and accuracy in identifying uropathogen in primary cultures. A direct urine testing should be optimized to reduce the diagnosing time, yet the limitation of these technologies is that the susceptibility of an antimicrobial cannot be provided. New promising technologies such as biosensors, micro fluidics, and other integrated platforms could show improvement in UTI diagnosis by detecting the pathogen directly from urine samples, rapid antimicrobial susceptibility testing, and point-of-care testing. But these are all experimental [28]. For the past 20 years,
certain tests have been approved to improve the diagnosis of bacterial infections [29,30]. Such as, as matrix-assisted laser desorption ionization–time of flight (MALDI–TOF) mass spectrometry, fluorescence in situ hybridization (FISH), and PCR. These tests require considerable sample processing in a clinical laboratory. Aiming to isolate the uropathogen from the urine matrix before analysis [31,32]. Efforts are directed to improve these technologies to facilitate the diagnosis of UTI directly from the urine sample. Theoretically, this might be possible and would further improve the clinical outcome compared to the traditional urine culture.

The use of MALDI–TOF, FISH, and multiplex PCR technologies in the lab, which is capable accelerating the identification of uropathogens, initial bacteria isolation is still a dependent factor, delaying bacterial identification by at least 12 hours. Adaptation of these technologies for direct-from-urine testing is the best route to expedite uropathogen identification for the future application of these techniques [33]. A balance between the time and cost of the diagnostic relative to what information is essential for treatment improvement should be considered in these advanced technologies for UTI diagnosis. To direct an appropriate therapy, it is essential to perform a screening urinary test to exclude negative samples in addition to a rapid molecular method to accurately identify the specific uropathogen (commonly Enterobacteriaceae family) coupled with a limited antimicrobial susceptibility of the common antibiotics. If the results were inconclusive using the above mentioned point-of-care testing, further analysis in a clinical laboratory would be needed [33].

**TREATMENT OF UTI**

The majority of UTIs are caused by Gram-negative pathogens, especially the Enterobacteriaceae families such as Escherichia coli, Klebsiella pneumonia, Proteus mirabilis and Enterobacter species [30,34-36]. UTIs that are caused by fungi are not as common as bacterial UTIs, but those who are with indwelling catheters, diabetes, or recent antibiotic use are at increased risk of fungal infection [37,38]. UTIs also can be caused by urogenital tuberculosis and parasitic organisms such as Schistosomahaematobium, although these infections are not commonly reported [39].

The selection of antibiotics can be made after identification of the uropathogen, putting in mind resistance rates, and adverse effects (Figure 2).
There were 3 RCTs published since 2000 comparing trimethoprim-sulfamethoxazole with other agents in young women with acute uncomplicated cystitis [40-42]. Among the trimethoprim-sulfamethoxazole susceptible group, the clinical cure rate was high. In contrast to those who had a trimethoprim-sulfamethoxazole resistant uropathogens (84% vs. 42% respectively; \( P < .001 \)). Thus, it is of importance to be aware of the local rate of trimethoprim-sulfamethoxazole resistance among community uropathogens because efficacy rate will differ accordingly. If the
local resistance prevalence cannot be estimated, individual risk factors, including the use of trimethoprim-sulfamethoxazole in the past six months or travel to an endemic area of resistance, can be used to anticipate resistance [43,44]. Trimethoprim-sulfamethoxazole is well tolerated drug with minimal side effects ranging between 1%-3% including nausea, diarrhea, headache, and dizziness [40,41]. In summary, it is recommended to use trimethoprim-sulfamethoxazole 160/800 mg twice daily for three days (level of evidence A-1) if the local resistance is less than 20% and if the clinical history does not suggest resistance [45].

**Nitrofurantoin**

In a recent randomized controlled trial of 338 women, a 5-day regimen of nitrofurantoin was as effective as the traditional 7-day course [40]. The clinical cure rate with nitrofurantoin and trimethoprim-sulfamethoxazole were similar in two meta-analyses studies [46,47]. Another Cochrane meta-analysis showed that the late clinical cure rate was also similar between those two agents (risk ratio, 1.01; 95% CI, 0.94-1.09) [47]. There was no significant difference in adverse events [47]. In summary, nitrofurantoin is an appropriate first line therapy (100 mg twice daily for 5-7 days). Its efficacy is comparable to the three day course of trimethoprim-sulfamethoxazole with the advantage of minimal resistance (level of evidence A-1). A 5-day regimen can be considered instead of 7 days by 1 RCT finding it comparable to three days of trimethoprim-sulfamethoxazole (level of evidence B-I) [40].

**Fosfomycin**

Six RCTs compared the efficacy of a 3-g single dose of fosfomycin trometamol with other antimicrobial agents for uncomplicated cystitis in which the clinical cure rate was comparable [48,49-53]. Two large double-blind RCTs compared the effectiveness of a nitrofurantoin for seven days with a 3-g single dose of fosfomycin found no significant difference in the clinical cure rate [48,49]. The efficacy and safety of fosfomycin was similar to other antibiotics in patients with cystitis in terms of clinical and microbiological success or adverse events occurrence [50]. In summary, to treat cases of uncomplicated cystitis, it is appropriate to consider fosfomycin trometamol 3 g in a single dose (level of evidence A-1).

**Fluoroquinolones**

The use of fluoroquinolones for the treatment of uncomplicated cystitis was studied thoroughly. Ten RCTs were found in that matter [41,51-59]. Overall, both clinical and microbiological effectiveness of fluoroquinolones is comparable with that of other first-line agents [54-60]. Although fluoroquinolones are highly effective agents for the treatment of uncomplicated cystitis, but the increasing resistance rate may hamper its use empirically (level of evidence B-III).

More recently, the U.S. boxed warning approved some changes to the labels of fluoroquinolone antibacterial drugs for systemic use either oral or intramuscular injections. Due to its association with disabling and potentially permanent side effects of the tendons (tendonitis or rupture),
muscles, joints, nerves, and central nervous system that can occur all together in the same patient. The risk of these serious side effects outweighs the benefits in patients with uncomplicated urinary tract infections. Other adverse reactions include; dizziness, insomnia, nervousness, somnolence, fever, rash, GI complaints, and AST/ALT elevation. Additional side effects of Levofloxacin include exacerbation of Myasthenia Gravis & it should be avoided in cases of weak respiratory muscles [61]. The FDA-approved fluoroquinolones include levofloxacin (Levaquin), ciprofloxacin (Cipro), ciprofloxacin extended-release tablets, moxifloxacin (Avelox), ofloxacin and gemifloxacin (Factive). The label contains a new limitation-of-use statement to reserve fluoroquinolones for patients who do not have other available treatment options for uncomplicated urinary tract infections [62].

**β-Lactams**

Trials has shown that the clinical and bacterial cure rates of β-lactams are lower than those of other antimicrobial agents [47,54,57]. When comparing the efficacy between the most appropriate antibiotics used for the treatment of UTIs, amoxicillin-clavulanate seems to be the least effective among all other antibiotics [63]. In summary, β-lactam agents have lower efficacy compared to other agents used for the treatment of UTI (level of evidence A-III).

**OTHER APPROACHES TO PREVENTION AND TREATMENT**

Several approaches have been investigated with limited evidence to support its use. These include; delayed antibiotic therapy, symptomatic treatment with NSAIDs, treatment with placebo, and treatment with cranberries [63]. In the setting of acute cystitis, no RCT reported any definite benefits. Neither for acute cystitis nor for prevention of UTI [64]. Suggestions of the recent evidence in recurrent UTI, cranberry products may be effective at reducing the risk of UTI, but data are conflicting [23].

Treatment of UTI with placebo has been considered in some RCTs [65-67]. Symptomatic cure at seven days was lower in the placebo group (42%) compared with the treatment group (70%), and some candidates developed pyelonephritis in 2.6%. Antibiotics were superior to placebo when measured by clinical improvement, cured clinically, or bacterial eradication. To summarize, available evidence does not support placebo treatment of adult, non-pregnant women who present with symptoms of acute cystitis; placebo is not helpful and may even be harmful (level of evidence A-III).

**Postcoital Antibiotics**

Recent studies show that sexual intercourse results in a higher incidence of symptomatic UTIs [68]. It is important to ask women about recent sexual intercourse, especially with new partners. Sexually transmitted infections (STIs) can cause urinary symptoms, and if vaginal discharge is present, an evaluation of STI is a must. Women are advised to void immediately after intercourse and to drink sufficient fluids. To prevent UTI in younger women a trial of postcoital antibiotic
prophylaxis is to be considered [69]. The postcoital prophylaxis option consists of a single dose of antibiotic taken within 2 hours of intercourse. This approach has a fewer side effect than daily prophylaxis antibiotics [70]. A single dose of nitrofurantoin, TMP-SMX after sexual intercourse is considered acceptable and most beneficial for women who experience UTIs within 24 to 48 hours after intercourse [71].

**Delayed Therapy and Ibuprofen Therapy**

Due to the dramatic increase in antimicrobial resistant pathogens, some investigators suggested the approach of treating UTI with anti-inflammatory agents (ibuprofen) which may control the woman’s symptoms and limit the overall use of antibiotics [72]. In a randomized trial of non-pregnant women with suspected acute cystitis subjected to 5 different management approaches [23]. The duration of moderate symptoms was similar among all, and 77% of women in the delayed antibiotics group ultimately received antibiotics. Besides, the women who delayed antibiotics for 48 hours or more had a 37% longer duration of symptoms [73, 74]. Some investigators from Germany did a trial and found that using ibuprofen 400 mg orally 3 times per day was not inferior to ciprofloxacin [23]. However, this RCT included 79 women with uncomplicated cystitis found no difference between those receiving ibuprofen vs. those receiving ciprofloxacin. It was concluded that 33.3% of patients received ibuprofen needed secondary antibiotic therapy compared to 18% among those receiving ciprofloxacin. In summary, to achieve a rapid relief of symptoms and an efficient recovery, it is recommended to use antibiotics to treat women with acute UTI symptoms. Any delay in initiating antibiotics therapy or using ibuprofen alone for symptomatic control may be harmful to the patient (level of evidence B-III).

**Estrogen Therapy**

Vaginal estrogen may be an effective prophylaxis measure for UTI in postmenopausal women. Oral estrogen therapy has not been found to be effective at reducing UTI risk compared with placebo. Two randomized studies showed that intra-vaginal estrogen is beneficial in postmenopausal women with recurrent UTI symptoms [75]. Estrogen changes the vaginal PH by lowering it. Thus, prolong the time to the first recurrence of UTI. Estrogen is well tolerated but certain side effects were reported by some patients such as; breast tenderness, PV spotting, bleeding of discharge and local burning or itching [75]. Thus, a prolonged use of antibiotics for 6 to 12 months and vaginal estrogen therapy can decrease UTI episodes, and to be considered in patients with recurrent UTIs [8].

**TREATMENT OF UTI IN SPECIAL PATIENT POPULATIONS**

Most of the studies on UTI treatment were performed in adult, non-pregnant, non-diabetic women with uncomplicated cystitis. The approach to UTI in men and women with diabetes is based on far more limited evidence [76]. One observational study found that diabetic women, in comparison with non-diabetic women, received a longer course of therapy, had a higher
recurrence rate within 30 days, and were more likely to be hospitalized for UTI [77]. However, the expert opinion addressed that diabetic women presenting with acute cystitis should be managed similarly to women without diabetes (level of evidence C-I). This recommendation does not apply to diabetic women with more severe presentations or with evidence of abnormal voiding.

**Bacteriuria in Pregnancy**

Pregnant women are at higher risk of asymptomatic bacteriurea (ASB) which is found to complicate 4-7% of pregnancies. It is well known that ASB is associated with adverse obstetric outcomes such as preterm delivery, low birth weight infants. In addition, the ASB may progress in 40% of the time to severe pyelonephritis if left untreated in pregnant women. It is recommended to treat bacteriurea in pregnancy using β-lactam antibiotics. Cefazolin or nitrofurantoin can be used for one week with a follow up visit to repeat urine culture. Prophylactic therapy may be considered in cases of recurrent episodes [78].

**Complicated UTI**

Treatment of complicated UTIs has become increasingly complex due to the rising prevalence of multidrug-resistant (MDR) gram-negative bacteria. Clinicians are advised to consider local resistance patterns during the selection of antimicrobial therapy [71].

**a. Zerbaxa:** This relatively new drug was approved by FDA three years back, in 2014. Zerbaxa has a combination of antibiotics (ceftolozane) and a beta-lactamase inhibitor (tazobactam). This combination aim to combat the bacteria and the enzyme produced by the bacteria to overcome resistance. A study comparing zerbaxa to levofloxacin, favored the latter in the clinical cure rate and bacterial eradication [79]. Resistance to the medication was found to be 2.7% compared to 26.7% among levofloxacin users. Common side effects included; diarrhea, nausea, headache, and fever [79].

**b. Avycaz:** Avycaz is a combination antibiotics therapy (ceftazidime-avibactam) which was approved by the FDA for the treatment of recurrent UTI under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act [80]. Avycaz is indicated in treating complicated UTIs caused by gram negative microorganisms including E. coli, Klebsiella species, and P. aeruginosa [81]. To maintain the effectiveness of these new drugs, and to reduce any chances for the development of resistance, it is recommended to reserve its use to treat patients with the susceptible bacteria for the exact agent [82,83].

**Recurrent UTI**

Recurrent UTIs (RUTI), defined by the presence of two or more infections in six months or three or more in one year is caused by, in most of the cases, similar pathogens to the sporadic infection [84]. These uropathogens ascend from the rectal flora to the bladder after colonizing the periurethral area and urethra [85].
Women with RUTIs should be counseled thoroughly regarding the features of re-infection and relapse. Supportive measures include drinking lots of fluids with frequent emptying of the bladder to flush the inhabitant bacteria. In addition to that, these women are encouraged to practice post-coital voiding, cleansing the genital area pre and post the sexual act with particular attention to wipe front to back direction, avoiding skin allergens, tight clothing, and bubble baths; and the choice of alternative forms of contraception rather than spermicides [11,70,86,87].

A variety of antimicrobials are used for the prevention and management of RUTIs [56,70,74,87-89,91-93]. A Cochrane review has shown that antibiotics in comparison to a placebo are more efficient in preventing recurrences in pre- and postmenopausal women with RUTIs [88]. Selecting the most appropriate antibiotic, it depends on patient’s pattern of resistance, adverse effects, interaction with drugs and cost. Nitrofurantoin or amoxicillin/clavulanic acid remain useful regarding bacterial sensitivity, but nitrofurantoin needs to be avoided in patients with pyelonephritis because of its reduced serum and tissue levels [85,94].

When simple measures fail, a prolonged course of prophylactic suppressive antibiotic is recommended. Low-dose antibiotics can be given daily for six months or longer. Some physicians advise prophylaxis on alternate nights or 3 nights per week [11,70,74]. Indications for a prolong continuous antibiotic prophylaxis therapy includes; women whom simple measures failed to treat UTI, women with frequent UTIs that cannot be attributed to a modifiable cause, or those at risk of complicated, recurrent UTIs [96]. Examples of suppressive therapies include the followings;

- Trimethoprim - Sulfamethoxazole 40/200 mg 3 times per week or single daily dose at bedtime
- Nitrofurantoin - 50-100 mg 3 times per week or single daily dose at bedtime
- Norfloxacin - 200 mg daily dose at bedtime or 3 times per week
- Trimethoprim - 100 mg at bedtime or 3 times weekly

**Probiotics** A strategy to restore host-supportive bacterial flora involves the use of probiotics. Probiotics are defined as live microorganisms which when administered in adequate amounts confer a health benefit to the host [97]. Individual strains of live microorganisms have been found to elicit specific inhibitory capacities on the growth of problem bacteria like MRSA and C. difficile [98-102]. Moreover, probiotics can exhibit a synergistic effect with antibiotics [102]. Probiotics can be regarded as the single most powerful alternative option under clinical development for the prevention and treatment of chronic infection [103]. Yogurts and other probiotic drinks are widely used over the counter therapies. They are considered as food supplements and their status is similar to herbal medicine. Moreover, the probiotics studies in the clinical trials had much more live microorganisms than those over the counter ones [104]. To date, insufficient data exist to support the routine use of probiotics in urological diseases such as RUTI or bladder cancer. But probiotics show promise in becoming an alternative or complementary treatment option for many diseases [104].
Box 1: American Heart Association Grading Scale and Level of Evidence*.

CONCLUSION

Urinary tract infection is a common presentation in clinical practice. It is among the most prevalent community-acquired and hospital-acquired infections, affecting almost 50% of the population at least once in their lifetime, accounting for considerable morbidity and health-care expenditure [30,34,35]. Women with UTI need to be properly investigated, and appropriate management should be individualized based on the presence of other risk factors. To establish a symptomatic UTI diagnosis, it requires a careful clinical and laboratory assessment using urinalysis and urine culture. The development of new diagnostic tools helps in identifying infections and recognizing an integration of the overall strategy to overcome the rise of drug-resistant pathogens [95]. Once a diagnosis is established, an antibiotic selection should be made by knowing causing organism susceptibility profiles, considering possible antibiotic side effects, possible interactions with other medications, and patient comorbidity. Although standard UTI therapy starts with antimicrobial therapy, alternative strategies are available to reduce exposure to antibiotics. This will result in maximizing success for UTI diagnosis and ensure wise choice of therapy while minimizing the risk of development of antimicrobial resistance.

References


63. FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. 2016.

82. FDA news release ; FDA approves new antibacterial drug Zerbaxa. 2014.
84. Forest Pharmaceuticals, Inc. package insert. 2015.
86. Gupta K, Trautner BW. Diagnosis and management of recurrent urinary tract infections in non-pregnant women. BMJ. 2013; 346: f3140.