# Outpatient antibiotic therapy for urinary tract infections in women

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■ Culture may not be required to confirm the diagnosis of urinary tract infections in young women with symptoms; antimicrobial therapy usually resolves symptoms. While relapse may occur more frequently with single-dose therapy, late recurrence rates are the same and side effects are less than with multiple-dose therapy. Patients with relapsing infection or frequent recurrence are candidates for chronic prophylaxis with low-dose antimicrobial or prompt self-administered therapy.

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THE CAUSE of community-acquired urinary tract infections (UTI) in young women is predictably *Escherichia coli*. In contrast, enteric gram-negative bacilli, including *E coli*, may be the cause of hospital-acquired UTI, but may be due to *Pseudomonas aeruginosa*, staphylococci, enterococci, and yeasts as well. Why the difference?

Hospitalized patients are generally sicker because of underlying disease, and often have indwelling urinary catheters and other invasive procedures of the urinary tract. In inpatients, systemic as well as local host defenses may be compromised. In the usual outpatient setting, it is a simple battle between the microbe and the host. Certain strains of *E coli* have virulence factors, including an ability to adhere to human uroepithelial cells and resist serum bactericidal activity.[1] Women who lack these factors seem peculiarly susceptible to UTI.

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## DIAGNOSIS

At one time, investigators made a distinction between cystitis and urethritis. However, frequent urination, urgency, dysuria, and pyuria are associated with any inflammatory process of the lower urinary tract.[2] Before ascribing such symptoms to UTI, vaginal or endocervical infections may need to be excluded by a pelvic examination and a KOH prep of vaginal secretions. The gold standard for diagnosis of lower UTI remains a "positive" urine culture from a properly collected and processed specimen. Any bacterial count may be significant, including counts below $10^2$–$10^3$ colony-forming units per milliliter of urine.[3] From a practical standpoint, however, most symptomatic patients have colony counts $\geq 10^4$.

## TREATMENT

It is not usually necessary to culture urine specimens of women who experience a first symptomatic episode of lower UTI. A prescription for an oral antimicrobial program will predictably result in cure in 80%–95% of cases. The principal question is how long should these patients be treated? Is single-dose therapy as efficacious

as multiple-dose therapy? Single-dose therapy is not new. Ronald and associates[4] reported in 1976 that a single intramuscular injection of kanamycin resulted in cure of 87% of well-documented lower UTI cases. Since then, very few of the various studies of the benefits of single-dose therapy have contained large numbers of patients randomized in carefully conducted prospective trials.

Several years ago my colleagues and I[5] reported such a study comparing single- and multiple-dose therapy with trimethoprim/sulfamethoxazole (TMP/SMX) in 136 young women. Sixty-eight patients received a single dose of three double-strength TMP/SMX tablets (160 mg/800 mg); relapses occurred in 10. Of 68 patients who received one double-strength TMP/SMX twice daily for 10 days, relapses occurred in only two. The difference was statistically significant ($P \leq .02$). However, 15 patients in both groups experienced reinfection at six weeks to six months after initial presentation. In addition, side effects of vaginitis and gastrointestinal distress were more common in multiple-dose treated patients. Neither pretreatment pyuria nor the presence of bacteria coated with antibody was predictive of recurrence. In fact, only five of 55 recurrences were detected by routine urine cultures during the six-month follow-up. If UTI recurred, it was invariably associated with symptoms. This prompted us to conclude that routine follow-up urine cultures in patients who remained asymptomatic after therapy are neither necessary nor cost effective.

In a recent study by Fihn and associates,[6] 216 young women who presented to a university student health center with symptomatic bacteriuria were randomized to receive single-dose therapy (two double-strength tablets of TMP/SMX) or a 10-day course of therapy of one double-strength TMP/SMX tablet twice daily. The therapy groups were similar for age, frequency of intercourse, number of male partners, previous UTI, and diaphragm usage. Investigators noted that both groups of patients became asymptomatic or markedly improved within three days after the onset of therapy. Among those with low colony counts ($10^2$–$10^4$), failure (i.e., positive cultures during or shortly after completion of treatment) occurred in 11% of the single-dose therapy patients and 16% of the multiple-dose therapy patients, which was not statistically different. However, those with colony counts $\geq 10^5$ were more likely to experience failure if they received single-dose (38%) rather than multiple-dose therapy (24%). Furthermore, the patients with a history of a recent UTI were more likely to experience failure with single-dose therapy (30%) *v* multiple-dose therapy (17%). Although infection recurred in 28% of diaphragm users compared to 16% of nonusers, the authors noted no difference in failure rates between the therapy groups.

As we noted in our study, Fihn and associates also observed more frequent adverse effects with multiple-dose therapy (25%) *v* single-dose therapy (12%). Early recurrence (or relapse; i.e., positive culture within six weeks of treatment with the same strain of microorganism) was also seen more often in their patients who received single-dose therapy. However, late recurrence was no different between the two therapy groups. The authors concluded that a 10-day course of therapy results in a higher immediate cure rate, but by six weeks there was no advantage to multiple-dose therapy. Early failure was explained by less effective eradication of vaginal *E coli* by single-dose therapy, resulting in more frequent same-strain recurrences. Because side effects are nearly twice as likely with a 10-day course of therapy, they suggested that a three-day course might be equally effective and less hazardous.

At the present time, there are no published studies comparing single-dose with intermediate-duration therapy.

### Appropriate single-dose therapy

The ideal subject for single-dose therapy is the young woman with urinary symptoms of less than seven days' duration and no evidence of upper urinary tract disease who is willing to return for follow-up if symptoms return. Single-dose therapy may predict the source of bacteriuria, since renal bacteriuria is more likely to relapse than bladder bacteriuria.

Single-dose therapy is less likely to produce antibiotic-resistant vaginal flora that may cause future symptomatic episodes.

Single-dose therapy is less expensive. Early relapse does not appear hazardous to the patient, provided that appropriate therapy is instituted promptly. In most cases, one would prescribe the same antimicrobial agent but continue therapy for 10–14 days.

Single-dose therapy is not indicated for any male patients with bacteriuria.

## PROPHYLAXIS

While the majority of women have no more than one or two episodes of symptomatic UTI per year, some are plagued by frequent recurrences. Those with at least four episodes a year are candidates for chronic antimicrobial prophylaxis. One must be aware that if reinfection oc-

curs during prophylaxis, it is likely due to a resistant bacterial species.

Patients should be monitored every three to four months for possible adverse drug effects and breakthrough bacteriuria. TMP/SMX in low doses has proven to be an excellent choice for chronic prophylaxis against recurrent UTI. One-half tablet of single-strength TMP/SMX is prescribed either nightly or every other night.[7]

Prophylaxis has no therapeutic effect because recurrence occurs with the same frequency after medication is stopped. Of interest, however, is the observation that recurrence is usually due to susceptible bacteria. For patients who cannot tolerate TMP/SMX, low-dose trimethoprim or nitrofurantoin (50 mg tablets) are satisfactory alternatives.

## DISCUSSION

When examining the various therapeutic and prophylactic options, physicians need to consider the patient's expense and convenience. For example, the cost of chronic prophylaxis for one year could be 10 times greater than self-administered single-dose therapy for four symptomatic episodes. Compliance with chronic prophylaxis could also be a problem, as well as the added expense of follow-up laboratory tests.

Appropriate strategy for successful management of lower UTI requires understanding of the patient's reliability—willingness to return in the event of recurrent symptoms—as well as knowledge of the clinical problem. Kunin[8] has recommended that the physician can be comfortable prescribing single-dose treatment for women who are reliable and have a low probability of upper UTI. On the other hand, women who are less reliable should be treated longer because they may have a higher probability of upper UTI due to increased likelihood of spread of infection if recurrent symptoms go unreported or if single-dosage treatment of recurrences is not self-administered promptly?

Upper urinary tract invasion is likely present when UTI recurs frequently in women. Therefore, recurrent UTI might best be treated with an initial four- to six-week course of therapy followed by a chronic prophylaxis program.

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