

THE EFFECTIVE PHYSICIAN

UTIs in Women

Background

The Infectious Diseases Society of America convened an international, interdisciplinary workgroup to update its 1999 guidelines regarding uncomplicated urinary tract infections in women. This guideline restricts its recommendations to premenopausal, nonpregnant women without urologic conditions or medical comorbidities.

Conclusions

Fully 75%-95% of uncomplicated UTIs reflect infection with *Escherichia coli*. Other common pathogens are mostly gram-negative such as *Proteus mirabilis* and *Klebsiella pneumoniae*. *Staphylococcus saprophyticus* is the more common gram-positive agent. Community-acquired methicillin-resistant *S. aureus* (MRSA) remains very rare.

The selection of antibiotics for uncomplicated UTIs should reflect patient presentation, allergies, and history of adherence in addition to local resistance patterns, drug cost, and tolerance to treatment failure.

The rise in resistant urinary pathogens in the ambulatory setting has complicated effective therapeutic treatment options, as well as mandated consideration of the ecologic impact of widespread use of antimicrobials for a commonly occurring infection.

Local resistance patterns based on hospital antibiograms often are not useful guides for ambulatory empiric therapy as the data are skewed by complicated inpatient infections and patients with substantial comorbid conditions.

Travel outside the United States or use of trimethoprim/sulfa in the preceding 6 months is a risk factor for resistance to trimethoprim/sulfa in patients with uncomplicated UTIs.

The low rates of resistance to nitrofurantoin and fosfomycin are felt to be secondary to their minimal



WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

DR. GOLDEN (left) is professor of medicine and public health and DR. HOPKINS is program director for the internal medicine/pediatrics combined residency program at the University of Arkansas, Little Rock. Write to Dr. Golden and Dr. Hopkins at obnews@elsevier.com.

effects on fecal flora.

Treatment with cephalosporins is associated with subsequent infection with resistant *Enterococcus* and other beta-lactam-resistant organisms.

Fosfomycin is active against many resistant organisms such as vancomycin-resistant *Enterococcus*, MRSA, and beta-lactamase-producing agents. The lack of clinical studies limits the strength of recommendations for use of this agent in patients with multidrug-resistant infections.

Implementation

Local prevalence of pathogen resistance greater than 20% to a specific antibiotic precludes that agent's use for empiric therapy of lower-tract infections.

Ampicillin or amoxicillin should not be used for empiric therapy of lower-tract infections because of their limited efficacy and high prevalence of pathogen resistance.

While a 3-day course of a fluoroquinolone is very effective for uncomplicated cystitis, this class of agent should be used for more complicated presentations to reduce the ecologic impact on community flora.

Nitrofurantoin, 100 mg b.i.d. for 5 days, is equivalent in efficacy to 3 days of trimethoprim/sulfa and represents an appropriate initial choice of therapy for cystitis because of low rates of resistance and a low impact on microbiologic flora.

If local resistance is under 20% of isolates, trimethoprim/sulfa, one double-strength b.i.d. for 3 days, is an

appropriate choice for empiric therapy of bladder infections.

While less effective than nitrofurantoin and trimethoprim/sulfa, a single 3-g dose of fosfomycin trometamol can be an appropriate choice because of resistance profiles and low ecologic impact.

Beta-lactam agents can be useful treatment agents for cystitis when other agents are not appropriate for a particular patient's presentation.

Nitrofurantoin and fosfomycin do not attain effective tissue levels in the kidney and should not be used in patients with cystitis who may also have pyelonephritis. Such patients often have bladder symptoms for nearly a week, unverified subjective fever, or vague flank discomfort.

Patients with suspected pyelonephritis always should have a culture and sensitivity to confirm appropriateness of therapeutic interventions.

A course of a fluoroquinolone antibiotic for 7 days, if local resistance is under 10%, is appropriate for empiric therapy of presumed upper-tract infections in ambulatory patients. If resistance is greater than 10%, fluoroquinolone therapy should start with an additional, single dose of a parenteral antibiotic such as a 1-g dose of ceftriaxone or an aminoglycoside to provide coverage while awaiting results of urinary culture.

Patients hospitalized for pyelonephritis should receive initial treatment with parenteral antibiotics. Aminoglycosides and beta-lactams may be more effective when combined with another agent for initial therapy of these upper-tract infection patients. ■

Reference

"International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women" (Clin. Infect. Dis. 2011; 52:e103-20).

Smoking Before First Childbirth Raises Breast Cancer Risk

BY MARY ANN MOON

FROM ARCHIVES OF INTERNAL MEDICINE

Smoking raises the risk of breast cancer modestly, a study has shown.

Several measures of smoking – including the current quantity of cigarettes smoked, the past quantity of cigarettes smoked, the age at smoking onset, the duration of smoking, and total pack-years of smoking – correlated with risk of breast cancer in an updated analysis of data from the Nurses' Health Study (NHS).

The strongest association was found in women who began smoking before giving birth for the first time, said Dr. Fei Xue of Brigham and Women's Hospital and Harvard Medical School, Boston, and associates.

There have been numerous previous studies of this issue, but they have yielded a mix of positive, inverse, and null associations. In what the investigators described as "the largest [study] so far on the association between smoking and breast cancer risk," Dr. Xue and colleagues assessed data on 111,140 women participating in the prospective NHS from 1976 through 2006.

VITALS

Major Finding: Women who were current or past smokers have a modestly higher risk of developing breast cancer than women who never smoked.

Data Source: An updated analysis of data collected on 111,140 subjects followed for 30 years in the Nurses' Health Study.

Disclosures: The Nurses' Health Study was funded by the National Cancer Institute. Dr. Xue and associates reported no relevant financial disclosures.

During that time there were 8,772 incident cases of breast cancer.

Women who had ever smoked had a "marginally increased" incidence of the disease compared with those who had never smoked, and the rate appeared to be comparable between current smokers and past smokers. "Every increase of 20 pack-years of smoking after menarche was associated with a marginal increase of incidence of breast cancer after adjusting for other risk factors," the researchers said.

Breast cancer risk was elevated in women who smoked 25 or more cigarettes per day either currently or in the past, women who began smoking at

or before the age of 17, and women who smoked for 20 years or longer. "In most of the previous studies, these smoking measures were not mutually adjusted. In [our] study, we created an index of active smoking that integrates quantity, age at which one started smoking, and duration of smoking.

"The results suggested that, although an elevated risk for light smokers and moderate

smokers was not apparent, heavy smokers who started smoking early in life, smoked for a long duration, and smoked a high quantity were at the highest risk of breast cancer, supporting an independent and additive effect from various smoking measures on breast carcinogenesis," they said (Arch. Intern. Med. 2011;171:125-33).

Starting to smoke before the first birth also was strongly linked with breast cancer. "All previous studies that have separately evaluated smoking before and after the first birth have found a similar pattern, suggesting that smoking before the first birth may be more important to breast carcinogenesis than smoking after the

first birth," Dr. Xue and associates wrote.

"Smoking before menopause was positively associated with breast cancer risk, and there were hints from our results that smoking after menopause might be associated with a slightly decreased breast cancer risk. This difference suggests an antiestrogenic effect of smoking among postmenopausal women that may further reduce their already low endogenous estrogen levels.

"Conversely, among premenopausal women, any antiestrogenic effect of smoking may not be strong enough to significantly reduce endogenous estrogen levels, leaving the dominant carcinogenic effect of smoking," the researchers said.

In contrast to active smoking, passive smoking in childhood or adulthood was not linked with breast cancer risk.

"Our results combined with the evidence from previous prospective cohort studies collectively suggest that passive smoking may not play an important role in the etiology of breast cancer. Nonetheless, we found that regular exposure to passive smoking may magnify the effect of active smoking," wrote Dr. Xue and colleagues. ■