

Nitrofurantoin, an Excellent Empiric Choice for Outpatient Cystitis

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We read with interest the report by Sanchez et al. describing antibiotic resistance among the 10 most common pathogens isolated from urine cultures in women in the outpatient setting (1). Resistance rates reflected in the over 1.6 million isolates reported may exceed the prevalence of resistance in cases of uncomplicated cystitis in which a urine culture is not collected (2). However, we felt that these data provide important insight into a common clinical question: when a woman presents with urinary tract infection (UTI) and a urine culture is indicated, which empirical antibiotic is most likely to be effective?

We used the data reported (1) to calculate a cumulative probability of susceptibility for each antibiotic (Table 1) by multiplying the percentage of resistance of each organism by that organism's fraction of all isolates and then summing those values and subtracting from 100%. For *Enterococcus faecalis*, resistances to ampicillin were used as the rates of resistance to amoxicillin-clavulanate; in all other cases, antibiotic resistance rates were presumed to be 100% if not reported.

We found that the cumulative probability of antibiotic susceptibility was driven primarily by the resistance pattern of *Escherichia coli*, which represented 65% to 80% of isolates. Nitrofurantoin showed high cumulative probabilities of susceptibility across all ages which were consistently higher than those to trimethoprim-sulfamethoxazole. The cumulative probability of trimethoprim-sulfamethoxazole resistance ranged from 22% to 33%. Rates of ciprofloxacin susceptibility were high among children but dropped with increasing age.

The 2010 Infectious Diseases Society of America (IDSA) guidelines for the treatment of uncomplicated cystitis recommend four empirical agents: nitrofurantoin, fosfomycin, pivmecillinam (not available in the United States), and, where resistance rates are less than 20%, trimethoprim-sulfamethoxazole (3). Fosfomycin use is limited by drug availability, cost, and lack of standardized susceptibility testing. The high trimethoprim-sulfamethoxazole resistance rates seen in this study call into question whether trimethoprim-sulfamethoxazole should remain a first-line agent for the treatment of cystitis in cases meriting a urine culture. The 2010 IDSA guidelines recommend reserving fluoroquinolones for more-severe infections, and the FDA issued a statement in May 2016 advising that the risks of fluoroquinolones generally outweigh their benefits for treating uncomplicated cystitis when other options are available (4). Finally, while urinary isolates retained high rates of susceptibility to beta-lactams and particularly to amoxicillin-clavulanate, concerns about inferior efficacy, increased collateral damage to the microbiome, and the spread of extended-spectrum-beta-lactamase-producing organisms prohibit beta-lactams from being recommended as first-line therapy.

The data presented by Sanchez et al. confirm that uropathogens in the community retain excellent susceptibility to nitrofu-

TABLE 1 Cumulative percentages of susceptibility among the 10 most common urine isolates from female outpatients in 2012

Antibiotic	% susceptibility in indicated age group (yrs)		
	Adults	Adults 65+	Children
	18–64	Adults 65+	0–17
Amoxicillin-clavulanate	93.2	90	95.1
Nitrofurantoin	92.5	86.9	94.4
Ceftriaxone	90.7	84.3	83.4
Cefuroxime	90.2	81.3	82.7
Ciprofloxacin	89	75	95.4
Trimethoprim-sulfamethoxazole	77.7	73.4	67.4
Cefazolin	59.2	47.5	52.9
Ampicillin	53	45.1	57.7
Oxacillin	1.3	0.9	1

rantoin even in women whose presentation merits a urine culture. Nitrofurantoin has urinary tract specificity, reaching high urinary levels but low plasma levels, and remains an excellent empirical choice when no prior culture results are available to guide therapy.

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