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Antibiotic Burden Associated with Treatment of Asymptomatic Bacteriuria

To the Editor—We read with interest the report by Kelley et al[1] entitled "Evaluation of an Antimicrobial Stewardship Approach to Minimize Overuse of Antibiotics in Patients with Asymptomatic Bacteriruira." These authors used an observational retrospective study design to evaluate the impact of an antimicrobial stewardship program (ASP) educational initiative on asymptomatic bacteriuria (ASB) management at their institution. Select components of the educational initiative included in-service presentations targeted at physicians and pharmacists, posting of notifications and memorandums, distribution of pocket cards, and daily review of antibiotics for the treatment of urinary tract infections (UTIs) by ASP members. They found a decrease in empirical antibiotic administration from 66 (62%) of 107 patients before the initiative to 28 (26%) of 107 patients after the initiative ($P < .0001$).[1]

We agree with the authors that treatment of ASB presents a significant problem. The Infectious Diseases Society of America (IDSA) guidelines regarding ASB recommend against treating adults with ASB except pregnant women and individuals undergoing urologic procedures.[2] Administration of antibiotics when not indicated may result in adverse drug reactions, development of antibiotic resistance, and *Clostridium difficile* infection.[3,4] Therefore, we have also taken steps to evaluate the management of ASB at our institution and estimate the added antibiotic burden resulting from the treatment of ASB, focusing on patients with an indwelling urinary catheter. We outline the results of our evaluation here.

A comparative observational study of catheterized patients with ASB was conducted. Retrospective medical record review was completed for patients who met the following inclusion criteria: (1) age 18–89 years; (2) admission to an internal medicine or surgery service between November 1, 2011, and November 31, 2012; (3) a urine culture containing 10^4 colony-forming units/mL bacteria or greater; and (4) a urinary catheter in place for 24 hours or more before the culture was obtained. Patients were excluded on the basis of documentation of 1 or more of the following symptoms of a UTI: temperature 37.9°C or more, costovertebral tenderness, dysuria, urinary frequency, urinary urgency, rigors, new onset delirium, and increased muscle spasticity in quadriplegic and paraplegic patients. Additional exclusion criteria similar to those used by Kelley et al[1] included pregnancy; medical history of a solid organ transplant; known urinary tract anatomical abnormality; renal stones; malignancy; foreign bodies of the urinary tract; being scheduled for genitourinary manipulation within 24 hours of culture; candiduria; death or hospital discharge before culture results were available; or current incarceration. Patients were considered to be treated for ASB if an antibiotic targeted at the bacteria isolated from the urine was administered within 5 days of culture obtainment. If a patient received antibiotics for other reasons, this was not categorized as ASB treatment. Demographic and clinical information was collected and summarized for treated and nontreated patients and univariate analysis was performed to describe characteristics associated with ASB treatment. Human subjects research approval was provided by the Office of Responsible Research Practices institutional review board.

Medical records of 228 patients with bacteriuria were reviewed; 194 patients met exclusion criteria. The primary reason for exclusion was the presence of signs or symptoms of a urinary tract infection. Of the remaining 34 patients included in the study, 22 (65%) were treated for ASB. Among treated and nontreated patients, there were no statistically significant differences in demographic characteristics, urinalysis, or urine culture results thought to drive antibiotic prescribing in patients with ASB (Table 1). The mean ($\pm$ standard deviation [SD]) duration of in-hospital antibiotic therapy was 3.5 $\pm$ 2.1 days, and the mean ($\pm$SD) planned duration of antibiotic therapy as documented in the patient discharge summary was 7.4 $\pm$ 4.2 days. This equated to approximately 7 days of unnecessary antibiotic exposure per patient with ASB. Three patients were tested for *C. difficile* within 30 days of urine culture obtainment, but no patients had a positive test result.

The majority of research published on the treatment of ASB has been performed in nursing homes, but 3 additional studies have been conducted in the acute care hospital set-

TABLE 1. Demographic and Clinical Variables in Catheterized Patients with Asymptomatic Bacteriuria

Variable	Treated (n = 22)	Not treated (n = 12)	P[a]
Age, years			
<61	11 (50)	5 (42)	.6418
≥61	11 (50)	7 (58)	
Sex			
Male	6 (27)	7 (58)	…
Female	16 (73)	5 (42)	
Comorbidities			
Diabetes mellitus	6 (27)	5 (42)	.4590
Paraplegia/quadriplegia	6 (27)	6 (50)	.2655
Immunodeficiency[b]	4 (18)	1 (8)	.6347
UTI within previous year	7 (32)	4 (33)	1.0000
Patient care service			
Medicine	17 (77)	10 (83)	…
Surgery	5 (23)	2 (17)	
WBC count on day of culture obtainment, cells/mL, mean ± SD	9.5 ± 5.1	9.7 ± 2.9	.6245
WBCs (UA)			
Absent	1 (5)	0 (0)	.9190
Rare, 1–9 cells/mL	5 (26)	4 (40)	
10–49 cells/mL	4 (21)	2 (20)	
≥50 cells/mL	9 (47)	4 (40)	
Bacteria (UA)			
Absent	3 (16)	5 (50)	.0834
Present	16 (84)	5 (50)	
Bacterial count, CFU/mL			
10,000–50,000	3 (14)	3 (25)	.7692
50,000–100,000	1 (5)	0 (0)	
>100,000	18 (82)	9 (75)	
Bacterial species isolated			
Non-ESBL-producing Enterobacteriaceae,	14 (64)	5 (42)	.0907
ESBL-producing Enterobacteriaceae	0 (0)	1 (8)	.3529
Nonfermenting gram-negative organisms	4 (18)	4 (33)	.4097
Gram-positive organisms	8 (36)	5 (42)	1.0000
Mixed microbes	2 (9)	1 (8)	1.0000
Catheter changed within 5 days of culture obtainment	8 (36)	4 (33)	…
Catheter removed within 5 days of culture obtainment	12 (55)	6 (50)	…

NOTE. Data are no. (%) of patients, unless otherwise indicated. CFU, colony-forming units; ESBL, extended-spectrum β-lactamase; SD, standard deviation; UA, urinalysis; UTI, urinary tract infection; WBC, white blood cell.

[a] Statistical analysis completed using χ^2 or Fisher exact tests for categorical variables and the Wilcoxon rank-sum test for continuous variables. All tests were 2-tailed with $P \leq .05$ considered statistically significant.

[b] Human immunodeficiency virus infection (CD4 cell count, <200 cells/mm^3), active malignancy and receipt of chemotherapy, immunosuppressive agents (azathioprine, cyclosporine, tacrolimus, sirolimus, and mycophenolate), or corticosteroids dose equivalent to 10 mg prednisone daily for ≥2 weeks.

ting.[5-7] The findings of these studies as well as our own findings and those of Kelley et al[1] demonstrate a 32%–65% treatment rate of ASB when ASP and ASB education are lacking, despite IDSA guideline recommendations.[1,2,5-7]

ASPs are critically important in combating the overuse and misuse of antibiotics. We commend Kelley et al[1] for the success of their ASP educational initiative at decreasing empirical antibiotic prescribing in ASB at their institution. However, additional factors that may influence antibiotic prescribing in ASB, such as urinalysis result, quantity of bacteria isolated, and bacterial species isolated, were not reported for each group, potentially limiting their evaluation. Our study attempted to evaluate some of these factors but was limited by the small sample size. Regardless of patient-specific factors that may influence practitioner decisions, ASPs should employ strategies to limit antibiotic prescribing in ASB. The ASP at our institution is currently taking measures to limit urine culture obtainment when not indicated.[8] This has involved

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refining criteria for reflex urine cultures on the basis of urinalysis and the implementation of evidence-based algorithms to guide urine culture obtainment. We urge other ASPs to make similar efforts to educate medical staff, reinforcing that bacteriuria should not be treated in the absence of symptoms.

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Hospital *Clostridium difficile* Infection Testing Rates: Is "Don't Ask, Don't Tell" at Play?

To the Editor—Interinstitution comparisons of infection rates rely on infection end points that accurately reflect true incident disease and that are consistently measured across centers. A recent article by Haley and colleagues[1] takes important steps toward improving the reporting on *Clostridium difficile* infection (CDI) rates. In their study of 3,458 reported hospital-onset CDI cases in 124 hospitals in New York state, they assess the potential for 3 measures (numerator audit, denominator correction, and age adjustment) to improve the accuracy of hospital incidence classification. Comfortingly, their original measure is relatively robust. Combined, these 3 measures do not result in much reclassification; 6% of hospitals are reclassified into higher risk groups, and 6% are reclassified into a lower risk group. Furthermore, the most influential of the 3 factors was denominator correction, and this correction is easy to implement: hospitals need only to use their information systems to subtract hospital-days of patient stays of less than 4 calendar-days. All in all, it is an easy message to relay to hospital systems instituting mandatory reporting of CDI rates: "mind your denominator!"[2] But should we really be consoled, or are there other issues with CDI reporting lurking below the surface?

We would like to point out a potential source of bias that has not been addressed in the literature on CDI reporting: CDI testing rates. Figure 1*A* shows a 14-fold variation in *C. difficile* testing rates (from less than 10 to 140 tests per 10,000 patient days) across tertiary hospitals in European countries that correlates strongly with CDI incidence ($R^2 = 0.64$; data retrieved from Bauer et al[3]). Now, this relationship may in fact reflect the higher incidence of CDI in high-testing countries, because increased test positivity may spur increases in testing levels.[4] However, as Figure 1*B* shows, there is no such correlation ($R^2 = 0.00$).

The National Healthcare Safety Network surveillance definitions attempt to standardize testing rates.[5] Specifically, all unformed stool specimens that are sent to the hospital laboratory are subjected to CDI testing, and repeat specimens obtained within 2 weeks are considered to be duplicates and not reported, but these measures do not specify who should or should not undergo testing. Are samples from all patients with diarrhea tested, or only a portion? And what is considered diarrhea?[6] These ambiguities suggest that the symptom severity threshold for initiating testing could vary significantly between institutions and wards. In addition, use of more