Asymptomatic Bacteriuria

To the Editor—Spivak et al [1] conclude correctly that, among veterans, asymptomatic bacteriuria (ASB) is commonly misdiagnosed as “urinary tract infection” (UTI) and treated unnecessarily, to the patient’s detriment. However, limitations in the definitions these authors used may undercut their important message and lead providers to disregard their findings.

Specifically, the study’s stated diagnostic criteria for cystitis, pyelonephritis, and ASB were nonstandard and inconsistent with the cited references. For cystitis, the authors required the presence of pyuria, which was not mentioned in the Infectious Diseases Society of America (IDSA) treatment guidelines from 1999 (in which bladder symptoms and a positive urine culture sufficed) or 2011 (which explicitly accepted the 1999 diagnostic criteria) [2, 3]. Acute cystitis clearly occurs without pyuria in some women [4]. For pyelonephritis, the authors required flank pain and/or tenderness plus fever, whereas the 1999 IDSA guidelines accepted flank pain (and/or tenderness) and/or fever. Fever is not a universally accepted criterion for pyelonephritis [5, 6]. Moreover, ASB presumably could be diagnosed based on a single urine sample, whereas for voided samples from women the IDSA ASB guidelines require a confirmatory culture [7], which is rarely done in clinical practice so was probably done in few of the study subjects, if any [1]. Consequently, many of the subjects whom the authors classified as having ASB, and therefore as not qualifying for antimicrobial therapy, had ≥1 symptom and/or physical finding suggestive of cystitis or pyelonephritis, per IDSA guidelines, or of urosepsis. Most clinicians would be reluctant to ignore such manifestations, and perhaps appropriately so. Indeed, the clinical trials underlying the IDSA ASB guidelines, which convincingly showed no benefit from treating ASB, involved asymptomatic individuals identified through prospective urine screening programs [7], not by urine cultures that providers ordered as part of routine clinical care, potentially in response to unexplained clinical manifestations—as occurred for many of the present study subjects [1].

It would be of interest to know what proportion of subjects had none of the manifestations listed by Spivak et al [1, table 2], including systemic inflammatory response syndrome criteria, and so were truly asymptomatic. It also would help to know how many had only the nonspecific, noninflammatory manifestations in that listing (ie, altered mental status, malaise, nausea, and lethargy). Such ambiguous manifestations, together with bacteriuria (with or without pyuria), would qualify them for the recently proposed label bacteriuria/pyuria of clinically undetermined significance (BPCUS) [8]. These 2 clinical entities—bacteriuria that is truly asymptomatic and BPCUS—represent the “low-hanging fruit” for which UTI-related antimicrobial stewardship efforts are most appropriate.

I fear that attempts to convince providers that bacteriuria is actually just ASB even when it is accompanied by localizing UTI symptoms and/or otherwise unexplained manifestations of systemic inflammatory response syndrome, and that such patients should not be treated, are doomed to failure; they also threaten the credibility of stewardship efforts and may even harm patients. Providers unquestionably tend to cast too broad a net in diagnosing and treating “UTI” [9], but we must avoid going reactively to the opposite extreme by casting too narrow a net.

Notes

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Reply to Johnson

To the Editor—We thank Dr. Johnson for his questions raised regarding our definitions used for asymptomatic bacteriuria (ASB), cystitis and pyelonephritis, and potential implications on interpretation of our data. Namely, he states we may have categorized some patients as ASB that in reality clinicians may be reluctant not to treat, thereby negating the significance of our findings. Specifically, (1) those with only 1 localizing symptom of cystitis and no pyuria on urinalysis (UA), and (2) those lacking ≥2 typical urinary symptoms in the absence of a UA. Additionally, he suggests our requirement of fever in addition to localizing symptoms for pyelonephritis is overly sensitive. We have attempted to address these concerns below.

There are no established gold standard diagnostic criteria for cystitis or pyelonephritis in males. Of note, the Infectious Diseases Society of America (IDSA) treatment guidelines for cystitis and pyelonephritis from 1999 and 2011 explicitly state they do not contain recommendations on urinary tract infections (UTIs) in men [1, 2]. At the time of the Medication Use Evaluation project development, we modified existing diagnostic criteria to arrive at a clinically meaningful population of patients most likely to have symptomatic UTIs. After initial review of the manuscript, we further stratified patients with ASB into those with and without systemic inflammatory response syndrome (SIRS) criteria in order to provide clarity to the reader as to which patients represent a sicker group of patients whom clinicians may treat empirically. Our population was predominantly male (93%), 95% of which had a UA performed with the majority (89% [1882/2109]) showing evidence of pyuria. Additionally, we excluded neutropenic patients who in theory may not have pyuria in the presence of a UTI. Therefore, it is unlikely we had significant numbers of patients with UTIs with only one typical urinary symptom in the absence of pyuria.

To better define the distribution of symptoms among our ASB cohort and address the possibility we mislabeled patients with UTIs as ASB, we analyzed the cohort of patients with ASB not meeting SIRS criteria (n = 729) and found 364 (50%) had no signs or symptoms listed in Table 2, 12 (2%) had one symptom of cystitis alone in the absence of pyuria on UA, and 265 (36%) had only symptoms listed in Table 2, 12 (2%) had one symptom of cystitis alone in the absence of pyuria. Additionally, 4% (36/961) of patients classified as ASB had flank pain and/or costovertebral tenderness alone, in the absence of fever. Therefore, a total 4.5% of patients with ASB met the 1999 IDSA guideline criteria for pyelonephritis and were potentially missed by our definition. The majority of patients classified as ASB either had no symptoms or nonspecific symptoms alone.

Based on these data, we stand by our conclusion that the majority of bacteriuria among inpatient Veterans likely represents ASB with significant opportunity for improved antibiotic use and overtreatment of ASB should be a major focus of antibiotic stewardship programs.

Note

Potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Ecological Fallacy, Nonspecific Outcomes, and the Attribution of Disproportionate Vaccine Benefits

To the Editor—In their recent publication, Luca et al [1] used an ecological design to compare all-cause pneumonia hospitalizations and associated costs in Ontario before (1992–2001) and after infant pneumococcal conjugate vaccine (PCV) availability—initially

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