Asymptomatic bacteriuria: review and discussion of the IDSA guidelines

Lindsay E. Nicolle *
Department of Internal Medicine and Medical Microbiology, University of Manitoba, Health Sciences Centre, Winnipeg, Canada

Abstract
Asymptomatic bacteriuria is a common finding, but is usually benign. Screening and treatment of asymptomatic bacteriuria is only recommended for pregnant women, or for patients prior to selected invasive genitourinary procedures. Healthy women identified with asymptomatic bacteriuria on population screening subsequently experience more frequent episodes of symptomatic infection, but antimicrobial treatment of asymptomatic bacteriuria does not decrease the occurrence of these episodes. Clinical trials in spinal-cord injury patients, diabetic women, patients with indwelling urethral catheters, and elderly nursing home residents have consistently found no benefits with treatment of asymptomatic bacteriuria. Negative outcomes with antimicrobial treatment do occur, including adverse drug effects and re-infection with organisms of increasing resistance. Optimal management of asymptomatic bacteriuria requires appropriate implementation of screening strategies to promote timely identification of the selected patients for whom treatment is beneficial, and avoidance of antimicrobial therapy where no benefit has been shown.

Keywords: Asymptomatic bacteriuria; Screening; Pregnancy; Management

1. Introduction
Asymptomatic bacteriuria, also referred to as asymptomatic urinary tract infection (UTI), is common [1]. There has been considerable controversy about the appropriate management of bacteriuria. Evidence reported in clinical trials undertaken over the past three decades, however, is sufficient to support recommendations for management in most populations. The optimal approach varies among different patient groups. Recently, the Infectious Diseases Society of America (IDSA) developed and published guidelines for screening for, and the treatment of, asymptomatic bacteriuria [2]. This paper provides a commentary on these guidelines, including a review of important recommendations.

The IDSA uses a standard rating system to describe the strength of recommendation and level of evidence. For strength of recommendation, ‘A’ means the recommendation is always valid; ‘B’ that it is valid in most cases, but there may be exceptions; and ‘C’ that it may or may not be appropriate.

The quality of evidence is judged by Roman numerals, ‘I’ for at least one prospective randomized comparative trial—the highest quality of evidence; ‘II’ for prospective cohort studies, or case-control studies; and ‘III’ for consensus of experts in the absence of appropriate clinical trials.

2. Historical background
Fifty years ago, Kass and other investigators first proposed and validated the use of the quantitative urine culture for the microbiological diagnosis of UTI [3,4]. Asymptomatic patients from whom bacteria were isolated in quantitative counts of \( \geq 10^5 \) colony-forming units (CFU)/mL in a voided urine specimen had the same organisms consistently isolated in paired specimens obtained by urinary catheterization. When lower quantitative counts of bacteria were isolated from voided specimens, the paired catheterized specimens were usually negative. The lower quantitative counts in voided specimens were interpreted as contamination.

Widespread acceptance and application of the quantitative urine culture identified several patient populations who...
were clinically asymptomatic but had a high prevalence of positive urine cultures [5]. These included, among others, pregnant women, individuals with urological abnormalities and patients with indwelling urethral catheters. Pyelonephritis was recognized as an important problem for pregnant women, and many early studies evaluated the impact of treatment of asymptomatic bacteriuria on pyelonephritis in pregnancy. These studies consistently documented that treatment of asymptomatic bacteriuria substantially decreased the risk of pyelonephritis later in pregnancy. The clear and consistent benefits of treatment of bacteriuria in this population were interpreted to be generally applicable, leading to endorsement of treatment of asymptomatic bacteriuria for other patient groups [4]. The conceptual framework for clinicians was that asymptomatic bacteriuria was consistently harmful in all populations and warranted antimicrobial treatment. The following several decades saw advances in understanding through critical clinical evaluation in selected patient populations. In particular, observations from long-term cohort studies and prospective randomized comparative trials in defined populations with asymptomatic bacteriuria have addressed appropriate management.

3. Diagnosis of asymptomatic bacteriuria (Table 1)

3.1. Urine culture

The diagnosis of asymptomatic bacteriuria in women requires at least two consecutive voided specimens with similar organism(s) isolated in sufficient quantitative counts [6]. This definition is derived from studies reporting that an initial voided urine specimen with a quantitative count of \( \geq 10^5 \text{CFU/mL} \) of organisms was confirmed only 80% of the time in a second specimen obtained within 1 week. A third voided specimen was consistent with the first two specimens 95% of the time [5]. The observation of only 80% positive concordance of the second specimen was interpreted as contamination of the initial specimen. In fact, transient bacteriuria is common in young women, and the finding of 20% of women with negative cultures on the second specimen probably reflects transient bacteriuria identified on the initial specimen, rather than contamination [7]. While two consecutive voided specimens with \( \geq 10^5 \text{CFU/mL} \) of the same organism isolated is the recommended standard for diagnosis in women, alternative definitions have been used in some studies. Bacteriuria has been identified with only a single voided specimen collected to minimize contamination with voided specimens are both uncommon in men. One study reported that a quantitative count of \( \geq 10^5 \text{CFU/mL} \) on a single voided specimen was reliable for identifying bacteriuria [10]. However, the number of participants with asymptomatic bacteriuria in this study was small—most men enrolled were symptomatic. Thus, the quantitative count of \( \geq 10^5 \text{CFU/mL} \) remains the appropriate microbiological criterion. In elderly men with voiding managed by external condom catheters, the requirement for a quantitative count \( \geq 10^5 \text{CFU/mL} \) has been validated by comparison with results of concurrent catheterized specimens [11,12]. Lower quantitative counts in specimens collected from these men reflect colonizing periurethral organisms or contamination of the condom, tubing or leg bag.

Criteria for identification of bacteriuria in specimens obtained from catheterized patients are similar for women and men [13]. Any quantitative count in a urine specimen obtained through a urinary catheter is consistent with bacteriuria. In practice, most laboratories will not identify quantitative levels of bacteriuria <\( 10^5 \text{CFU/mL} \), but counts as low as \( 10^2 \text{CFU/mL} \) may be relevant from catheterized specimens. When \( \geq 10^5 \text{CFU/mL} \) of an organism are isolated from urine collected through an indwelling catheter, the level of bacteriuria consistently achieves quantitative levels of \( \geq 10^3 \text{CFU/mL} \) within 24–48 h [14]. It is not known whether the lower quantitative counts represent bacteria present in the bladder urine or small numbers of organisms in the catheter that subsequently ascend to the bladder to establish bacteriuria.

3.2. Pyuria

Pyuria is inflammation within the genitourinary tract and is a common accompaniment of asymptomatic bacteriuria. The prevalence of pyuria varies among different patient groups (Table 2). Healthy schoolgirls and women with bacteriuria have associated pyuria about 50% of the time [7]. Individuals with underlying genitourinary abnormalities, including elderly residents of institutions or those with chronic indwelling catheters, consistently have associated pyuria [17]. The degree of pyuria in elderly bacteriuric women corre-
lates with localization of infection—the number of leucocytes in the urine is increased with upper UTI [17]. The presence or degree of pyuria has not, however, been shown to have prognostic significance [21–23]. Thus, pyuria has no apparent clinical relevance in those with asymptomatic bacteriuria, and should not influence decisions about antimicrobial therapy.

4. Recommendations to treat (Table 3)

There are few patients for whom treatment of asymptomatic bacteriuria is appropriate. As screening to identify asymptomatic bacteriuria is only relevant if treatment is indicated, screening for asymptomatic bacteriuria should also be restricted to patients for whom treatment has been shown to be beneficial.

4.1. Pregnant women

The evidence that supports a recommendation for screening for, and treatment of, asymptomatic bacteriuria in pregnant women is consistent and compelling. Treatment of asymptomatic bacteruria identified early in pregnancy decreases the risk of pyelonephritis later in pregnancy by at least 75% [2]. Treatment of asymptomatic bacteriuria also significantly improves the adverse foetal outcomes of premature labour and low birth weight [24]. The benefits of treatment of asymptomatic bacteriuria in pregnancy were identified early following widespread implementation of the quantitative urine culture as a reliable diagnostic test for bacteriuria. Screening for, and treatment of, asymptomatic bacteriuria in early pregnancy has been a standard of practice for many decades in most developed countries. This intervention has been so successful that pyelonephritis is now a relatively uncommon complication of pregnancy, and the continued relevance of screening for bacteriuria is occasionally questioned. More recent reports describing the implementation of routine screening programmes for bacteriuria in prenatal clinics in Spain and Turkey (where screening had not previously been standard practice) shows a decrease in the rate of pyelonephritis for screened populations consistent with earlier studies [25,26]. A cost evaluation using American data reported that screening for and treating pyelonephritis is appropriate if the prevalence of asymptomatic bacteriuria is greater than 2%, and the incidence of pyelonephritis greater than 13% [27]. Given that the prevalence of asymptomatic bacteriuria in pregnant women is 4–7% and the risk of pyelonephritis with bacteriuria is 25–30%, this intervention remains cost-effective.

Screening for bacteriuria in pregnant women requires a urine culture. Screening for pyuria is insensitive, and identifies only about 50% of pregnant women with bacteriuria [15]. There are several other operational issues for management in pregnancy where definitive recommendations cannot be made because available information is insufficient. A Swedish study reported that 18 weeks was the optimal time for a screening culture to maximize the identification of bacteriuria [28]. However, in North America the current practice is to screen at the end of the first trimester, usually at 12 weeks. It has not been evaluated whether a second culture confirming bacteriuria should be obtained after an initial positive culture. Current practice is, often, to provide antimicrobial treatment following a single positive urine specimen. Clinical trials that support the recommendation for screening and treatment usually identified bacteriuria with at least two consecutive specimens. Some women will have transient bacteriuria, so obtaining a second culture to confirm persistent bacteriuria may limit antimicrobial exposure in pregnancy. Finally, some women acquire bacteriuria later in pregnancy after initial negative screening urine cultures. This may occur in as many as 1–2% of pregnant women, and these women are at risk of pyelonephritis in later pregnancy. It has not been evaluated whether a second screening culture obtained later in pregnancy could further reduce the risk of pyelonephritis and its complications, and remain cost-effective.

Table 3

<table>
<thead>
<tr>
<th>Recommendation</th>
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<tr>
<td>Pregnant women should be screened for bacteriuria by urine culture at least once in early pregnancy, and they should be treated if the results are positive</td>
<td>A-I</td>
</tr>
<tr>
<td>Screening for, and treatment of, ASB before transurethral resection of the prostate is recommended before other urological procedures for which mucosal bleeding is anticipated</td>
<td>A-III</td>
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4.2. Urological procedures

Evidence to support treatment of asymptomatic bacteriuria prior to selected urological procedures is also convincing, although interpretation of reported clinical trials is less straightforward. Prospective, randomized clinical trials report that treatment of asymptomatic bacteriuria prior to transurethral resection of the prostate (TURP) decreases postprocedure bacteriuria and sepsis [29–32]. The antimicrobial regimens evaluated in these studies varied in antimicrobial...
5.1. Healthy women

The prevalence of asymptomatic bacteriuria is 2–5% in healthy, premenopausal women [1]. Bacteriuria is often transient, although some women may have bacteriuria persistent for months or even years. Long-term, prospective, cohort studies report that women with bacteriuria identified at an initial screening are more likely to be bacteriuric at subsequent surveys, and also experience an increased frequency of symptomatic urinary infection. However, a prospective, randomized trial of treatment of asymptomatic bacteriuria with nitrofurantoin or placebo did not demonstrate any benefits of antimicrobial treatment [35]. After 1 year, the prevalence of bacteriuria and the incidence of symptomatic infection were similar in treated and placebo groups. Thus, biological variables that promote symptomatic urinary infection in healthy women also appear to facilitate asymptomatic bacteriuria, but asymptomatic bacteriuria is not directly attributable to subsequent symptomatic episodes. Cohort studies with follow-up at 15 or 24 years have not identified any long-term negative outcomes attributable to bacteriuria for pre- or postmenopausal women [36,37].

5.2. Diabetic women

Diabetic women have been reported to have an increased prevalence of bacteriuria relative to age-matched nondiabetic women, although the biological explanation for this observation is not clear [16]. In large surveys in female diabetic populations, the prevalence of bacteriuria is reported to be 7–9%, but the prevalence is higher in some smaller studies enrolling a more selected group of patients [38]. Women with diabetes and bacteriuria are characterized by a more prolonged duration of diabetes and long-term complications such as neuropathy, but not by abnormal parameters of diabetic control, such as glycosylated haemoglobin [16]. A prospective randomized comparative trial of treatment or nontreatment of bacteriuria for up to 3 years, with continuing screening and treatment, identified no benefits with antimicrobial treatment of bacteriuria in diabetic women [22]. Women randomized to antibiotic therapy, however, had five times more antibiotic days for any indication, and a significantly higher number of adverse events attributable to antimicrobial agents given for treatment of symptomatic or asymptomatic urinary infection. Long-term, prospective, cohort studies also report no adverse outcomes attributable to asymptomatic bacteriuria in diabetic women [39].

Table 4

<p>| Recommendation against screening for, and treatment of, asymptomatic bacteriuria (2) |</p>
<table>
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<tr>
<th>Recommendation Level</th>
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<tr>
<td><strong>Screening for, and treatment of, asymptomatic bacteriuria is not recommended for</strong>:</td>
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<tr>
<td>1. Premenopausal, nonpregnant women</td>
<td>A-I</td>
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<tr>
<td>2. Diabetic women</td>
<td>A-I</td>
</tr>
<tr>
<td>3. Older people living in the community</td>
<td>A-II</td>
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<tr>
<td>4. Elderly, institutionalized people</td>
<td>A-I</td>
</tr>
<tr>
<td>5. People with spinal cord injury</td>
<td>A-I</td>
</tr>
<tr>
<td>6. Patients with indwelling catheters</td>
<td>A-II</td>
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There is strong evidence to support a recommendation not to screen for or treat asymptomatic bacteriuria in other populations where asymptomatic bacteriuria is a common finding.

5. Recommendations not to treat (Table 4)

There are also many residual questions addressing the optimal management of screening for, and treatment of, bacteriuria prior to a urological procedure. How long before the procedure should a urine culture be obtained? If a culture is obtained early, the infecting organisms may change prior to the procedure, compromising optimal antimicrobial selection. A specimen obtained 3 days prior to the procedure will allow culture results to be available at the time of the procedure and seems a reasonable recommendation, but has not been validated. How long before the start of the procedure should antibiotics be initiated? If started too early, superinfection with a more resistant organism may occur prior to the procedure. Antimicrobial therapy has been reported to be effective when initiated immediately before the procedure [33], and this seems a reasonable recommendation for initiation pending further evaluation. Finally, how long should antimicrobial therapy be continued after the procedure? Treatment of asymptomatic bacteriuria in this context is not to cure bacteriuria, but to prevent the complication of sepsis. Continuing the administration of antimicrobial agents only for the duration of the procedure is as effective as more prolonged therapy in achieving this goal [33]. However, some studies report that continuing antimicrobial therapy until the indwelling catheter is removed decreases the risk of postoperative infection, although much of this is asymptomatic infection [34].

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5.3. Elderly residents of institutions

Elderly institutionalized populations have an extraordinarily high prevalence of bacteriuria [17]. In these residents, the prevalence of bacteriuria correlates with the level of functional impairment. Prospective, randomized, comparative trials of treatment or no treatment of asymptomatic bacteriuria have consistently reported no benefits with antimicrobial treatment of bacteriuria in these populations [40–43]. Treatment of asymptomatic bacteriuria does not decrease symptomatic episodes or the prevalence of bacteriuria, and chronic genitourinary symptoms such as chronic incontinence are not improved. Furthermore, treatment of bacteriuria does not improve survival. Adverse outcomes do occur with antimicrobial therapy and include adverse drug effects, recurrent infection with more resistant bacteria, and increased costs. Thus, there is convincing evidence from clinical trials to support nontreatment of bacteriuria in institutionalized elderly people.

5.4. Spinal-cord injury patients

The prevalence of bacteriuria in spinal-cord injury patients is high, irrespective of the technique used for bladder emptying [44]. The incidence of symptomatic infection is relatively low given this high prevalence of bacteriuria. Two prospective, randomized comparative trials of antimicrobial treatment or no treatment report no benefits for treatment of spinal-cord injury patients [45]. However, the study numbers were small and follow-up was relatively short. The recommendation for nontreatment is, however, also supported by studies documenting that re-infection, usually asymptomatic, occurs promptly after treatment of asymptomatic bacteriuria, and re-infecting strains are of increased resistance [46].

5.5. Patients with indwelling catheters

Prospective, randomized, comparative trials of the treatment of asymptomatic bacteriuria [47] or funguria [48] in patients with indwelling catheters have consistently identified no benefits of treatment. There is, however, increased re-infection with resistant organisms following treatment. One study of the treatment of bacteriuria that persisted 48 h after catheter removal reported a lower rate of symptomatic infection 2 weeks following catheter removal [49]. The proportion of participants experiencing symptomatic infection within 2 weeks was 17% in placebo recipients, but zero in the participants who received treatment. This study enrolled a selected group of relatively young women with short-term catheterization for gynecological indications. Older women enrolled in this study were less likely to have bacteriuria clear up spontaneously or remain free of bacteriuria following antimicrobial therapy. The generalizability of the observations from this study to other populations following catheter removal is not known. In addition, the relative risks and benefits of delaying treatment until symptoms develop compared with uniform treatment of all patients with bacteriuria have not been evaluated.

6. Unresolved issues

There are many questions relevant to the management of asymptomatic bacteriuria that require further evaluation. Some issues addressing pregnant women or patients undergoing urological procedures have already been discussed. A complex problem in elderly institutionalized people is the accurate diagnosis of symptomatic infection, given the consistent high prevalence of bacteriuria in these populations [17]. Clinical assessment is problematic because of impaired communication and chronic symptoms accompanying chronic diseases. Further studies are needed to address the question of when it is appropriate to treat the bacteriuric resident of a long-term care facility who has clinical deterioration but no localizing genitourinary findings in order to support optimal clinical care and antimicrobial use in these populations.

Screening for bacteriuria prior to elective implantation of prosthetic orthopaedic devices, with treatment of bacteriuria prior to surgery if present, is sometimes recommended. This practice is based on the reported association of infection at any site prior to surgery having an increased likelihood of postsurgical site infection. However, there is no evidence that asymptomatic bacteriuria is causative for such infections. Prophylactic antimicrobial agents to prevent postsurgical surgical site infection are uniformly prescribed for these procedures, and these antimicrobial agents are frequently effective in clearing bacteriuria, at least temporarily. In fact, one retrospective study that directly addressed this question reported no increased risk of surgical site infections with asymptomatic bacteriuria [50]. Thus, there is little evidence to support screening and treatment prior to prosthesis insertion, but clinical trials specifically addressing this question have not been reported.

The clinical implications, if any, of pyuria in selected bacteriuric populations could be further characterized. The associations of bacteriuria and treatment outcomes with antimicrobial agents for patients with chronic kidney disease are not well described [51]. The natural history and appropriate management of long-term indwelling urinary devices other than urethral catheters, such as ureteric stents and nephrostomy tubes, also require further systematic study. In elderly, noncatheterized populations, persistent infection with Proteus mirabilis and other urease-producing organisms has not been reported to be associated with adverse outcomes from urolithiasis. However, whether persistent P. mirabilis bacteriuria in younger women or men requires alternative management is not known. The appropriate management of asymptomatic bacteriuria in immunocompromised patients is also not well described. The most highly immunocompromised patients—those undergoing bone marrow and solid organ transplants or chemotherapy with prolonged
neutropenia—uniformly receive prophylactic antimicrobial agents. This prophylaxis is effective in preventing both symptomatic and asymptomatic urinary infection, as well as other infections, and additional benefits of screening for bacteriuria are not clear.

7. Conclusions
There has been continued progress in understanding the epidemiology, natural history and management of asymptomatic bacteriuria. For most populations with a high frequency of asymptomatic bacteriuria, there is now good evidence from clinical trials to direct management strategies. There are, however, many remaining questions to be addressed in additional clinical trials. There is also a challenge to achieve appropriate practice based on current evidence, such as to address the dual goals of maximizing patient safety and limiting antimicrobial use.

References