Reducing Treatment of Asymptomatic Bacteriuria

What Works?

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KEYWORDS

• Asymptomatic bacteriuria • Diagnostic stewardship • Antimicrobial stewardship
• Bacteriuria guidelines • Bacteriuria in the elderly

KEY POINTS

- Asymptomatic bacteriuria is very common for some populations.
- Practice guidelines for management of bacteriuria should be followed.
- Urine cultures should not be obtained from persons for whom there is no indication for the treatment of bacteriuria.
- Multidisciplinary antimicrobial stewardship programs evaluated in different health care settings report variable success in decreasing urine cultures and avoiding inappropriate antimicrobial therapy, but may be resource intensive.
- Some populations with a high prevalence of bacteriuria at any time, such as persons with voiding abnormalities or elderly subjects with acute delirium or dementia, require development and evaluation of further population specific approaches to support practices to minimize inappropriate antimicrobial therapy.

INTRODUCTION

Asymptomatic bacteriuria, defined for most populations as the isolation of potentially pathogenic organisms in quantitative counts $\geq 10^5$ cfu/mL ($\geq 10^8$ cfu/L) from urine of individuals without localizing genitourinary signs or symptoms attributable to urinary infection, is a common finding (**Table 1**).[1] Clinical observations and clinical trials evaluating treatment of asymptomatic bacteriuria for diverse populations support a benefit with treatment only for pregnant women or for persons undergoing an invasive urologic procedure anticipated to be associated with bleeding.[1] However, in populations for whom a benefit of treatment has not been shown, a positive urine culture often leads to antimicrobial therapy. Thus, a positive urine culture drives inappropriate antimicrobial treatment which provides no clinical benefit for the patient but contributes to

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Table 1
Populations addressed in guidelines for antimicrobial treatment for asymptomatic bacteriuria[1]

Population	Prevalence of Bacteriuria
Screen and treat for bacteriuria	
Pregnancy	2%–10%
Prior to invasive urologic procedures	40%–60%
Do not screen or treat for bacteriuria	
Healthy children or adults	≤2%–5%
Elderly women or men in community or nursing home	Community: W 4%–19%; M 1%–16% Long-term care: W 25%–50%; M 15%–50%
Persons with diabetes	W: 11%–16%; M: 0.7%–11%
Persons with renal transplant	Post-transplant: 1 mo: 23% 21 mo: 10%–17% 23% and 10%–17%
Persons with impaired voiding following spinal cord injury (intermittent catheter)	23%–69%
Persons with indwelling urethral catheter	Short term: 3%–6% increase/day Long term: 100%
Persons undergoing elective non-urologic surgery	
Persons with surgery for or living with implanted urologic devices	18%–45%
No recommendation	
High risk neutropenia (<100 cells, ≥7d)	Low
Persons with indwelling catheters at time of catheter removal	Variable

Abbreviations: M, men; W, women.

negative outcomes attributable to antimicrobials, including adverse drug effects or drug interactions, increased antimicrobial resistance, *Clostridium difficile* infection, and increased costs.

Development and implementation of strategies to support the optimal management of asymptomatic bacteriuria have become a standard of care for health care settings in developed countries as requirements for antimicrobial stewardship programs in health care delivery have been implemented. These programs recognize that the management of asymptomatic bacteriuria may require distinct considerations and strategies for different populations, given the variability in frequency and causes for bacteriuria, persons affected, and limitations in clinical assessment for some important patient groups, such as the elderly with dementia or subjects with voiding abnormalities. Interventions and programs implemented in clinical settings as stewardship strategies with the goal of improving management of asymptomatic bacteriuria have been reported to have variable success.

Follow Practice Guidelines

The Infectious Diseases Society of America Clinical Practice 2019 Guidelines for the Management of Asymptomatic Bacteriuria[1] updated earlier recommendations and summarized current evidence. These guidelines were developed in collaboration

with other national organizations and have been widely endorsed. They are the foundation for the development of programs to optimize the management of asymptomatic bacteriuria.

Treatment of asymptomatic bacteriuria in pregnant women prevents pre-term delivery which may be precipitated by early onset of labor complicating third trimester pyelonephritis. For individuals who undergo an invasive genitourinary procedure anticipated to be associated with bleeding, sterile urine at the time of surgery prevents postprocedure bacteremia and sepsis. Bacteriuria treatment in this situation is consistent with preoperative surgical antimicrobial prophylaxis for any operation in a contaminated field. These 2 patient groups, for whom treatment is indicated, are easily identified and efficiently managed in the context of routine prenatal or urologic care. Apart from some limited populations where there is insufficient evidence to support a recommendation (high-grade neutropenia, at time of indwelling catheter removal), other persons with asymptomatic bacteriuria do not benefit from antimicrobial treatment of bacteriuria and, for some, treatment may be harmful[1] (see **Table 1**). A positive urine culture, however, drives antimicrobial therapy, often irrespective of patient symptoms. Thus, a urine specimen for culture should not be obtained unless there is an indication for antimicrobial treatment if a positive urine culture is reported. Pyuria often accompanies bacteriuria, but in the absence of symptoms attributable to a positive urine culture, it is not an indication for antimicrobial treatment in a person with bacteriuria who is otherwise asymptomatic.[1]

A straightforward intervention with implementation of the guidelines is the identification of practices in the community or health care facilities where screening of urine specimens is being undertaken in patients for whom treatment is not indicated. The discontinuation of inappropriate routine screening can promptly decrease inappropriate treatment, usually requires limited resources, and is often sustainable. In a report from 1 teaching center, removing routine urinalysis and urine culture from the preoperative testing checklist for patients undergoing cardiac artery bypass graft surgery resulted in an immediate and sustained 87% decrease in urine cultures obtained and 50% fewer prescriptions given for bacteriuria.[2] Identification and discontinuation of such "routine" urine cultures is a priority intervention for antimicrobial stewardship given the relative ease of implementation, limited resource requirements, potential substantial impact, and durability. Other populations identified in the guidelines for whom routine screening could be discontinued include other non-urologic elective surgical patients, transplant patients, persons with diabetes, asymptomatic persons with short-term or long-term indwelling catheters, and long-term care facility residents who are clinically stable.[1]

Diagnostic Stewardship

Diagnostic stewardship is described as "coordinated interventions with particular attention to the integration of laboratory and molecular diagnostics at an earlier point in care to facilitate improved patient management."[3] This includes strategies to limit collection of urine specimens where there is no patient benefit, restricting laboratory processing for culture of urine specimens received by the laboratory, and limiting reporting of positive culture results. These interventions are important aspects of an overall antimicrobial stewardship initiative. The implementation and effectiveness of diagnostic stewardship contributions to an antimicrobial stewardship program are addressed more fully in another article.[4]

Some specific diagnostic stewardship interventions have been reported to be effective and are important stewardship initiatives relevant to asymptomatic bacteriuria.[3,5] These include practices such as not processing specimens from asymptomatic

patients where there is no indication for treatment, implementation by the laboratory of a practice of reflex urine culture, where only urine specimens positive for pyuria on screening are processed for culture, or not reporting positive urine culture results without clinician confirmation that the patient is symptomatic. Some of these interventions are efficiently implemented at the laboratory level and have a potential for substantial and sustained impact in decreasing reports of positive urine cultures for patients who do not require antimicrobial therapy. In a randomized trial of modified reporting of urine culture results which compared standard laboratory reporting to a requirement for physicians in the intervention arm to contact the laboratory for organism and susceptibility results of a positive culture, appropriate treatment was 80% in the modified arm and 53% in the standard reporting arm.[6] A multicenter, quasi-experimental study reported that implementation of a reflex urine culture strategy for urine specimens received by the laboratory decreased processing for urine culture by 76%.[7] Patients who were pregnant, neutropenic, aged less than 1 year, renal transplant recipients, or undergoing urologic interventions were excluded. However, while implementing the specific strategy of a reflex urine culture may lead to a substantial decrease in urine cultures and unnecessary antimicrobial use in some populations, it is much less useful for populations where bacteriuria is also usually accompanied by pyuria, such as the elderly in long-term care. In these populations, obtaining a urine culture based on the presence of pyuria may lead to increased diagnosis of urinary infection based on a positive culture and contribute to inappropriate antimicrobial treatment.[8]

Antimicrobial Stewardship

Antimicrobial stewardship programs have been mandated for hospitals and other health care settings in many developed countries. Components of these programs are incorporated into national standards for hospitals, nursing care centers, and ambulatory care centers. Optimizing management of asymptomatic bacteriuria is recognized as an important activity of antimicrobial stewardship. The implementation and impacts of stewardship initiatives to limit the use of antimicrobials for the treatment of asymptomatic bacteriuria when not indicated have been described in many reports which encompass a spectrum of acute health care settings, including emergency rooms,[9,10] hospital wards,[5,11] and ambulatory outpatient settings[12] (**Table 2**). Some antimicrobial stewardship programs have been developed regionally with implementation across multiple facilities in a given geographic area[13] or health care system[11] to promote streamlining of resources and wider regional standardization of practices.

Stewardship programs are usually multimodal, and may be relatively resource intensive. Practices to optimize management for asymptomatic bacteriuria are often embedded within a more comprehensive program which addresses stewardship for other types of infections. Programs described for acute and long-term care primarily focus on education of health care providers and case audits of antimicrobial prescriptions with feedback.[5] Best practices are generally developed with input from a team of relevant professionals including physicians, nurses, pharmacists, and laboratory personnel, and finalized following review and input from affected practitioners. The frequency of obtaining urine cultures and antimicrobial treatment of bacteriuria and urinary infection are monitored for adherence to guidelines, sometimes including interventions by the review team to alter antimicrobial therapy. Metrics that are reported for monitoring may include proportion of urine cultures requested which are not appropriate, proportion of subjects inappropriately treated for bacteriuria, frequency of stewardship interventions to modify treatment, and frequency of adverse antimicrobial effects. To improve efficiency and consistency some programs use institutional

Table 2
Multimodal stewardship programs to promote non-treatment of asymptomatic bacteriuria in a spectrum of health care settings

Study	Setting	Interventions	Effectiveness
Hitchins et al,[9] 2023	Emergency room, discharged patients, positive urine culture, no antibiotic	ASB assessment protocol	Antibiotics: 50% vs 87% ($P < .0001$) 30-d admissions: 7% vs 8% (NS) 30-d ED visits: 14% vs 16%
Grigoryan et al,[13] 2022	4 Veterans Affairs health centers	Case-based teaching to apply algorithm distinguishing UTI or ASB	Urine cultures: NS for intervention overall ↓ 3.24/1000 beds for difference in difference Antibiotics: ↓21.7% (P=.007) Duration antibiotics: ↓21% ($P = .001$)
Cash et al,[10] 2022	Emergency room,	Physician/pharmacist sessions; pocket cards treatment algorithms; alerts; elimination of reflex urine culture	Patients with pyuria and ASB inappropriately treated: pre 100% post 32.4% Sustained at 3 y: (28%)
Rehan et al,[14] 2022	Long-term care, single center	Modified reporting of positive urine cultures	Appropriate treatment, modified vs standard: 61 vs 51% ($P = .33$) Untreated ASB: 41% vs 27% (P=.25)
Shah et al,[11] 2021	Medical–surgical unit	In-service providers, nurses, pharmacists, and pharmacist and nursing interventions	ASB treatment: 62%–6% (0.16–0.72; $P = .003$)
Salem-Schatz et al,[15] 2020	Long-term care, 31 facilities	QI workshops, webinars, coaching calls	Baseline, first, second incident rate ratios: urine culture: 0.74 (0.83, 0.63) UTI diagnosis: 0.73 (0.86, 0.60) *Clostridium difficile*: 0.56 (1.61, 0.45)

Abbreviations: ASB, asymptomatic bacteriuria; ED, emergency department; QI, quality improvement; UTI, urinary tract infection.

electronic decision support systems for these programs.[16] Features of these electronic systems have included pop-up messages, passive messages accompanying an order, and a "nudging" order set to guide therapeutic approaches.

Most reports describe effectiveness as an analysis of before and after surveys, with some reports of randomized comparative trials. Programs vary from single interventions to multiple components. For example, Hitchens and colleagues[9] described a

single-center change in practice where patients with positive urine cultures after an emergency visit, who were deemed to have asymptomatic bacteriuria by the nurse reviewing follow-up cultures together with the clinical record, were not referred by the nurse to the physician for treatment assessment, and not contacted for follow-up. Follow-up treatment of patients with positive urine cultures decreased from 87% to 50% with this single intervention. Cash and colleagues[10] describe a single-center, retrospective, experience implementing a multicomponent emergency room stewardship program to decrease antimicrobial treatment of asymptomatic bacteriuria or pyuria. Interventions included physician and pharmacist presentations, pocket cards, treatment algorithms, electronic alerts, and elimination of reflex culture. Antimicrobial treatment for bacteriuria within 72 hours of the emergency visit decreased from 100% to 32% and was sustained 3 years later. Shah and colleagues[11] reported that a program of education together with pharmacy and nursing intervention in a 340-bed community hospital decreased treatment of asymptomatic bacteriuria from 62% to 22%, but did not address sustainability. Grigoryan and colleagues[13] reported outcomes of a quality improvement initiative for acute and long-term care wards in 4 Veteran's Affairs facilities which included case-based teaching of an evidence-based algorithm to distinguish urinary infection from asymptomatic bacteriuria together with support from a centralized coordinating center and a site-based internal facilitator. In an interrupted time-series difference in differences analysis, they reported a significant decrease in urine cultures of 3.24/1000 bed days, accompanied by a 21.7% decrease in antibiotic prescriptions and 21% decrease in duration of antibiotics.

These programs, generally, but not universally, report success in decreasing inappropriate urine cultures and antibiotic use, but the reported effectiveness is variable.[5] Despite the relatively consistent report of positive outcomes, the impact is often limited—an improvement of 20% to 50% is relatively modest—and highlights the magnitude of inappropriate treatment. Outcomes of these reports are not as compelling as those reporting the effectiveness of some of the laboratory-based initiatives or single interventions targeting 1 element of practice. The sustainability of programs is also unclear given competing resource needs with other programs. Advani and colleagues[5] have critically reviewed the components, complexity, and impacts of antimicrobial stewardship programs for asymptomatic bacteriuria stewardship in acute care facilities. They identify the spectrum of program components implemented and discuss the relative impact of these, which range from strong systems-based interventions, such as suppression of urine culture results, to weaker interventions that focus on physician education alone. Their conclusion was that optimal urine culture stewardship strategies ultimately require both technical interventions, such as those of diagnostic stewardship, and socio-adaptive interventions, such as those focusing on clinician education, as well as long-term, iterative feedback, for sustainability.

Antimicrobial Stewardship in Long-Term Care Facilities

Limiting inappropriate antimicrobial use for urinary infection in older persons with asymptomatic bacteriuria, particularly the elderly in long-term care facilities (see **Table 1**), is an important objective of antimicrobial stewardship but has been problematic to achieve.[17] The high prevalence of bacteriuria, approaching 50% or higher in functionally and neurologically impaired elderly, means a positive urine culture is common for any clinical presentation. The presence of chronic genitourinary symptoms, such as incontinence, together with limitations in communication and physical assessment given the high frequency of chronic neurologic diseases and functional impairment,

limits clinical assessment for the diagnosis of symptomatic urinary infection. Nonspecific, non-localizing symptoms, including fever, deterioration in mental or functional status, increased incontinence, or falls, are frequently attributed to urinary tract infection when a urine culture is positive, and treated with antimicrobials. Limited clinical trials and evaluations report these "nonspecific" presentations are not improved with antimicrobial therapy and should not be attributed to urinary infection.[1,18]

Antimicrobial stewardship programs developed for long-term care facilities include guidelines which recommend not screening for or treating bacteriuria in elderly residents with dementia or functional impairment unless clinical symptoms are consistent with urinary infection.[17] In a randomized controlled trial of the single intervention of modified reporting of positive urine culture results for long-term care facility residents where organism identification and antimicrobial susceptibilities for a positive culture were only reported if the physician contacted the laboratory to request them, a modest decrease of only 10% in inappropriate antimicrobial treatment in the intervention arm use was reported, and the difference between the intervention and nonintervention arm was not significant.[14] Salem-Schatz and colleagues[15] report experience with a statewide quality improvement program implemented to improve antimicrobial use in nursing homes in Massachusetts. The intervention was characterized as a learning collaborative which focused on increasing awareness of current guidelines to not treat in the absence of symptoms consistent with urinary infection. The program was supported through workshops, webinars, and coaching calls. There were 31 facilities participating in an initial 3 month collaborative with 17 providing sufficient information for analysis, an inter-collaborative period when the program was not offered, and a second collaborative period with 34 participating facilities and 25 submitting sufficient data. They reported significant improvements in urine culture, urinary infection, and *C difficile* rates (see **Table 2**) with implementation of the program. However, these improvements were modest and the relatively high proportion of facilities not submitting sufficient data makes it difficult to assess the overall effectiveness of the program or the utility of any specific components.

An explorative qualitative study using semistructured interviews was undertaken in long-term care facilities in 4 northern European countries (Poland, Netherlands, Norway, Sweden) to identify themes which could inform interventions to improve management of urinary infection in the elderly in these facilities.[19] There were 5 themes identified which influenced decisions to treat for suspected urinary infection: the clinical situation; diagnostic factors such as asymptomatic bacteriuria and complexity of diagnosis for the frail elderly; knowledge and attitudes; communication with colleagues, the patient, and family; and the context and organization of care. The broad coverage of these themes speaks to the complexity of addressing antimicrobial treatment for urinary infection in these populations. The findings from this qualitative study informed the development of a prospective, cluster randomized clinical trial with a multifaceted antimicrobial stewardship intervention of a decision tool for appropriate antibiotic use supported by a toolbox with educational materials including sessions for education, evaluation, and local tailoring of the intervention.[20] There were 43 general practices and 43 older adult care organizations participating in the prospective study. Antibiotic treatment for urinary infection was 0.27/person-year in the intervention group and 0.58/person year in the control group (rate ratio 0.42; 0.26–0.68). No differences were observed between the 2 groups in the important clinical outcomes of incidence of complications, hospital referrals, hospital admissions, mortality in 21 days, or overall mortality. The benefit was much stronger for patients with dementia (0.3; 0.17–0.64) than those without dementia (0.56; 0.28–1.12), and weaker in patients with urinary incontinence (0.24; 0.16–0.54 with and 0.53; 0.29–0.96 without). This relatively

resource-intensive approach provided some benefit, but sustainability was not addressed.

Another multicenter European study, in Denmark,[21] reported a cluster randomized controlled trial in 22 nursing homes which evaluated a tailored intervention to improve knowledge about urinary infection through interactive educational sessions and use of a dialog tool, compared to continuing standard practice for treatment of urinary infection. The adjusted outcome rate ratio was 0.42 (0.31–0.57) for receiving an antibiotic. There were no differences in all-cause hospitalization or mortality between the 2 groups. Thus, the reported effectiveness of this program was similar to the study reported by Hartman and colleagues.[20]

Despite these thoughtful and carefully implemented multimodal stewardship interventions, a substantial proportion of antimicrobial treatment for urinary infection in these settings was still considered inappropriate in the intervention arms, and the sustainability of the programs is unknown. Mylotte[17] provides a recent critical review addressing the complexity and lack of specificity of diagnosis of urinary infection in the nursing home resident. He identifies 8 decision tools or algorithms for identifying urinary infection in these settings which have been proposed for use over the past 2 decades and concludes there is no evidence that implementing any of these diagnostic tools has had an impact on the inappropriate treatment of urinary infection in elderly nursing home populations. One key factor contributing to this is the lack of an agreed upon "gold standard" definition for symptomatic urinary infection in this population. His conclusion is that the primary focus of any antimicrobial stewardship program for these facilities should be a reduction in the frequency of urine cultures, as it is the positive urine culture which drives antimicrobial therapy. Thus, there remains a need for further development and evaluation of antimicrobial stewardship approaches to limit the inappropriate treatment of asymptomatic bacteriuria in elderly residents of long-term care facilities.

SUMMARY

Initiatives to improve practices for management of asymptomatic bacteriuria have been widely mandated and implemented across different health care settings and populations. Some limited interventions, such as no routine screening of patients for whom there is no indication for treatment of asymptomatic bacteriuria, are relatively straightforward to implement, and may provide a substantial and sustained impact. In other settings, more complicated, multimodal programs are effective in limiting treatment of asymptomatic bacteriuria, but implementation requires multiple interventions. These programs are more resource intensive with less impact, and the sustainability is not well described. To further improve stewardship, it seems that additional or more innovative approaches will be needed. Studies of the potential role of inflammatory urinary markers other than pyuria to provide objective evidence of symptomatic or asymptomatic infection have not identified any diagnostic markers more definitive than pyuria alone, so implementation of further diagnostic laboratory approaches is not helpful. It will be interesting to evaluate whether approaches which incorporate artificial intelligence tools in some settings may have a role in addressing these challenges.

CLINICS CARE POINTS

- Screening for bacteriuria should be limited to populations where treatment of asymptomatic bacteriuria will provide a clinical benefit for the patient.

- Identifying and discontinuing non-beneficial routine urine specimens for culture is an intervention which may lead to prompt and sustained improvement.
- Some diagnostic stewardship modifications at the specimen collection or processing level may provide immediate and sustained improvements for the management of asymptomatic bacteriuria.
- Multimodal programs have been shown to decrease screening and inappropriate antimicrobial use, but improvements reported have often been modest; resources and sustainability need to be addressed to understand long-term benefits.
- Further interventions tailored to specific unique patient groups may be effective but require further evaluation.

DISCLOSURE

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