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Approach to a Positive Urine Culture in a Patient Without Urinary Symptoms

Barbara W. Trautner, MD, PhD^{1,2} [Investigator] and Larissa Grigoryan, MD, PhD³

Barbara W. Trautner: trautner@bcm.edu

¹Health Services Research Center of Excellence, Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas 77030, USA

²Department of Medicine, Section of Infectious Diseases, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, US

³Department of Family and Community Medicine, Baylor College of Medicine, Houston, TX, USA

Abstract

Asymptomatic bacteriuria (ASB) is a condition in which bacteria are present in a noncontaminated urine sample collected from a patient without signs or symptoms related to the urinary tract. ASB must be distinguished from symptomatic UTI by the absence of signs and symptoms compatible with UTI or by clinical determination that a nonurinary etiology accounts for the patient's symptoms. ABU is a very common condition that is often treated unnecessarily with antibiotics. Pregnant women and persons undergoing urologic procedures expected to cause mucosal bleeding are the only two groups with convincing evidence that screening for and treating ASB is beneficial. Randomized, controlled trials of ASB screening and/or treatment have established the lack of efficacy in premenopausal adult women, diabetic women, patients with spinal cord injury, catheterized patients, older adults living in the community, and elderly institutionalized adults. The overall purpose of this review is to promote an awareness of ASB as a distinct condition from UTI and to empower clinicians to withhold antibiotics in situations in which antimicrobial treatment of bacteriuria is not indicated.

Keywords

Asymptomatic bacteriuria; urinary tract infection; anti-bacterial agents; guidelines implementation

Introduction

Definition of ASB

In most patient populations, interpretation of a positive urine culture depends upon the presence or absence of associated symptoms. The definitions that we will use in this review are those of the Infectious Diseases Society of America (IDSA) guidelines concerning ASB (2005) and catheter-associated urinary tract infection, or CAUTI (2010).¹⁻² In a patient without signs and symptoms of urinary origin, the presence of bacteria in a non-contaminated urine specimen is defined as asymptomatic bacteriuria (ASB).³ In contrast,

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urinary tract infection (UTI) requires the presence of urinary-specific symptoms or signs in a patient who has both bacteriuria and no other identified source of infection.^{1,4} The definition of ASB requires isolation of the same organism in two consecutive voided urine specimens for women, one voided urine specimen for men, and, in addition, from a single urine specimen collected via urinary catheter in both sexes.² Neither the type of bacterial species isolated from the urine nor presence of pyuria can be used to determine whether the patient has ASB or UTI. Available evidence supports screening for and treatment of ASB in pregnant women and in patients undergoing invasive urologic procedures.³ In most other patient groups, there is convincing evidence that neither screening nor treatment lead to improved clinical outcomes.³ Unnecessary antibiotics given to treat ASB can cause harm in terms of antibiotic resistance, adverse drug effects, and wasted expense.⁵

These definitions are hard to apply in clinical settings, particularly in the patient populations in which ASB is most common—catheterized patients, nursing home patients, and patients in intensive care units. The lack of specific diagnostic tests to distinguish UTI from ASB means that the diagnosis of ASB entirely on clinical assessment of the patient's symptoms or lack thereof. Many hospitalized or institutionalized patients may be unable to express their symptoms, and non-urinary symptoms are often attributed to bacteriuria in such patients.⁶⁻⁸ Another challenge is that the diagnosis of ASB requires that the clinician ignore powerful stimuli for the use of antimicrobial agents, namely a positive urine culture result and pyuria. Other incorrect mental cues, such as reliance on urine color or urine odor, may also lead to misdiagnosis.⁹ Human microbiome studies are disproving the dictum that normal bladders are sterile,¹⁰ but the conviction that untreated bacteriuria will lead to harm persists.¹¹

This review will focus on the epidemiology of ASB and its clinical significance. The review will cover appropriate management of ASB in various patient populations, delineating where evidence is not adequate to support recommendations and discussing what evidence is able to guide the clinician in these areas of uncertainty. We will also summarize the growing body of published interventions that have been employed to prevent overtreatment of ASB. We will not address ASB in children, as the pathogenesis differs from that of ASB in the adult.¹² Furthermore, this review does not discuss symptomatic UTI or acute cystitis, which requires treatment with antibiotics to relieve symptoms¹³ and can lead to pyelonephritis when untreated.¹⁴ Asymptomatic funguria, management of ASB in patients undergoing urologic surgery, and management of ASB in renal transplant patients will be addressed in other chapters in this issue. The overall purpose of this review is to promote an awareness of ASB as a distinct condition and to empower clinicians to withhold antibiotics in situations in which antimicrobial treatment of bacteriuria is not indicated.

Epidemiology and Significance of ASB

ASB is very common

In 2008 the Centers for Disease Control published new surveillance definitions for CAUTI to be used by the National Healthcare Safety Network (NHSN), the United States' most widely used healthcare-associated infection (HAI) tracking system. In keeping with the increased awareness of the distinction between UTI and ASB, ASB was excluded from urologic conditions to detect and report, in contrast to earlier definitions.¹⁵ Presumably, the decision to exclude ASB was based on the growing awareness that ASB is not a clinically relevant condition in most populations. Changing the definition, however, was not accompanied by any change in the proportion of positive urine cultures treated with antibiotics in a large, academic medical center; such change is unlikely without an active intervention.¹⁶ Unfortunately, the current lack of standards for detecting and reporting ASB means that published epidemiology of this condition in the United States is based on data collected prior to 2008¹⁷⁻¹⁸ or is from smaller studies.¹⁹⁻²⁰ Prior to this definition change, a

point prevalence study in Veterans Affairs nursing homes in 2007 found that ASB accounted for 10% of all nursing home acquired infections, second only to UTI and skin infections.¹⁷ National surveillance data from 1990 through 2007 showed a significant decline in ASB rates in all ICU types.¹⁸ Estimated declines in ASB incidence ranged from 28.5% (95% CI, 20.1%-35.9%; medical/surgical without a major teaching affiliation) to 71.8% (95% CI 68.0%-75.2%; medical/surgical with a major teaching affiliation). These declines suggest that CAUTI prevention efforts in some ICUs may reduce ASB as well as CAUTI.

Risk factors for asymptomatic bacteriuria include older age, female sex, and abnormalities of the genitourinary tract (Box 1). For example, the prevalence of ASB in healthy young women is 1-5%, while women older than 70 years living in the community have a risk > 15%.²¹ Genetic factors may predispose certain women to ASB.²² In men, a higher post void residual is associated with asymptomatic bacteriuria, and older men are at higher risk for prostatic enlargement, which in turn creates a higher post void residual.²³ Whether diabetes itself creates a predisposition to ASB is not entirely clear. A single center study in 511 diabetic and 97 non-diabetic subjects (97) found a similar incidence of ASB in both groups.²⁴ However, a meta-analysis of 22 studies of ASB in diabetic versus non-diabetic subjects brought more depth to this topic. The point prevalence of ASB was higher in both women (14.2 vs. 5.1%; 2.6[1.6–4.1]) and men (2.3 vs. 0.8%; 3.7[1.3–10.2]) with diabetes than in healthy control subjects.²⁵

In patients with indwelling urinary catheters, the most important risk factor for bacteriuria is the duration of catheterization.²⁶ Antimicrobial agents decrease the risk of bacteriuria for initial 4 days of catheterization but are not of benefit and predispose to resistant organisms in patients catheterized longer than 4 days.²⁷ Since NHSN surveillance for CAUTI by definition includes only patients with indwelling catheters (Foley catheters), the risk of bacteriuria with other catheter types is not well-documented. A study in 7,866 inpatients on acute medicine and nursing home units over the course of one year documented 1,009 catheter-associated, positive urine cultures. Of these, 376 (37.3%) were from external (condom) catheters, and more of the urine cultures collected from condom catheters were positive than those collected from indwelling catheters (77.1% versus 55%, respectively, $P<0.001$).²⁸ Strategies to reduce CAUTI by substituting external catheters for indwelling catheters could inadvertently lead to increased antimicrobial overuse for ASB if the risk of bacteriuria with condom catheters proves to be a general phenomenon.

Clinical outcomes associated with ASB

Studies of the clinical impact of ASB are often confounded by the differences between persons who do and who do not have ASB at baseline. For example, 490 generally healthy women were included in a prospective study to assess the association between bacteriuria and renal function; of these, 48 had *E. coli* bacteriuria at baseline. Over a mean of 12 years of follow-up, no association was found between *E. coli* bacteriuria and a decline in renal function.³⁰ A subsequent analysis in generally the same cohort found that *E. coli* bacteriuria at baseline was associated with development of hypertension, but even at baseline, the *E. coli* bacteriuria group had a higher incidence of hypertension.³¹

Application of modern molecular typing techniques to samples from a prior trial of treatment versus non-treatment of ASB in diabetic women³² offers insight on why treatment of ASB is ineffective and even potentially harmful in this population.³³ Women with diabetes and *E. coli* bacteriuria were randomized to treatment for ASB (every 3 months) or no treatment. Among the 57 women in the treatment group, 76% treatment regimens were followed by recurrent *E. coli* bacteriuria, most of which (64%) involved a new strain of *E. coli*. Women in the treatment group received an average of 3 courses of antimicrobial therapy, but some were treated up to 15 times. Antimicrobial treatment did not prevent

recurrence but instead resulted in strain change over. A similar phenomenon was reported in a prospective study of 330 community dwelling women 80 years old, followed with serial urine cultures.³⁴ 40% of women with ASB carried the same strain of *E. coli* for 18 months, but antibiotic treatment led to strain turnover. Spontaneous strain turnover was also common, suggesting re-colonization. In this study, the women with ASB at baseline were more likely to have symptomatic UTI over the following 24 months than those without ASB ($P=0.019$), but the only confounding variable explicitly considered in analysis was age.

Overtreatment of ASB is very common

Failure to recognize ASB as a distinct condition from UTI has negative clinical consequences, namely overuse of antibiotics. These consequences include “collateral damage” or ecological adverse effects of antibiotic use, as well as the risks of cumulative antibiotic exposure to the individual patient.^{5,35-36} In 2013 the American Board of Internal Medicine identified treatment of ASB as one of the top 5 excessive healthcare practices in the field of geriatrics in its “Choosing Wisely” campaign.³⁷ The CDC “Get Smart: Know When Antibiotics Work” campaign promotes conservative use of antibiotics, including using antibiotics to treat infection but not colonization; ASB in this context would be considered bladder colonization.³⁸ The cumulative impact of antimicrobial overuse on the antimicrobial susceptibility of human pathogens impairs the effectiveness of current and future antimicrobial agents.³⁹ In a two-year Swedish community study, restriction of trimethoprim-containing drugs did not lead to any change in the trimethoprim resistance rate in *E. coli*, thus raising the ominous concern that antimicrobial resistance may be irreversible.⁴⁰

Unfortunately, mismanagement of ABU—or inappropriate treatment with antibiotics—is an epidemic condition.⁴¹ Multiple studies from the United States and Canada have evaluated how often patients with ASB receive antimicrobial agents for suspected UTI (Table 1). All have found substantial rates of overtreatment, ranging from 20% in an emergency room study⁴² to 83% in a nursing home setting.⁴³ A number of these studies reported high rates of overtreatment in catheterized patients, illustrating how difficult it is to interpret a positive urine culture in this population. Another concern is that many of the days of antimicrobial therapy given for ASB are unnecessary. In one study in catheterized inpatients, 201 (69%) of 293 days of antibiotic therapy to treat the urine were unnecessary.⁴⁴ A three-year retrospective study of patients with vancomycin-resistant enterococci in their urine documented that over 200 days of antimicrobial therapy were not indicated, resulting in \$50,000 in unnecessary antimicrobial costs.⁴⁵

Management of ASB

Patient groups with ASB who should be routinely be treated

Current guidelines recommend ASB screening and treatment in pregnant women and patients undergoing selected urologic procedures.^{2,46} A recent meta-analysis comparing antibiotics versus no treatment for pregnant women with ASB found that the treatment substantially reduced the risk of pyelonephritis.⁴⁷ The relationship between ASB, low birth weight and preterm delivery is less well established.⁴⁸ In a Cochrane review, antibiotic treatment was associated with a reduction in the incidence of low birth weight but not with preterm delivery.⁴⁷ However, poor methodological quality of studies included limits the strength of conclusions from this meta-analysis. Moreover, the definition of prematurity has changed since the 1960s, when the majority of these studies were conducted. Three more recent observational studies reported an increased risk of preterm birth with ASB in pregnancy.⁴⁹⁻⁵¹ An ongoing Dutch trial is evaluating whether nitrofurantoin treatment of

low-risk, pregnant women with ASB is effective in reducing the risk of preterm delivery and/or pyelonephritis and adverse neonatal outcome.⁵²

There is no consensus in the literature on screening frequency, the duration of therapy or the choice of antibiotic for ASB in pregnancy.⁴⁸ A Cochrane Review of different antibiotic regimens to treat ASB in pregnancy found five comparative trials, four of which tested currently used antimicrobial agents: fosfomycin, cefuroxime, pivmecillinam, ampicillin, cephalexin, and nitrofurantoin.⁵³ Each trial examined a different antibiotic regimen, so no conclusions can be drawn about the most effective antibiotic regimen for ASB of pregnancy. However, in the most recent and largest of these five studies a 7-day course of nitrofurantoin was shown to be more effective at achieving bacteriologic cure at 14 days post-treatment than a 1-day course of nitrofurantoin.⁵⁴ In another Cochrane review on the treatment duration for ASB, the cure rate was higher for the four-to seven-day treatment than for the one-day treatment.⁵⁵

Patient groups with ASB who should not be treated

- Non-pregnant women
- Diabetic women
- Elderly persons living in the community
- Persons with spinal cord injury
- Catheterized patients while the catheter remains in place

Several prospective studies had established that ASB in premenopausal, non-pregnant women is not associated with long-term adverse outcomes and treatment of ASB neither decreases the frequency of symptomatic infection nor prevents further episodes of ASB.² More recently, a randomized, non-placebo controlled trial studied ASB specifically in women with recurrent UTI. This study enrolled 673 women ages 18-40 with recurrent UTI and ASB at baseline.⁵⁶ Women were split into two groups, treated with a single course of antibiotics or not treated, and followed for 12 months. At the last follow-up, 41 (13.1%) in the untreated group and 169 (46.8%) in the treated group had a symptomatic UTI (RR, 3.17; 95% CI, 2.55–3.90; $P < .0001$). This finding is in line with a prior observational cohort study that reported women who had received antimicrobials during the previous 15-28 days were at higher risk for UTI.⁵⁷ A plausible explanation is that antibiotics may predispose to UTI by altering the flora colonizing the vagina.

Randomized, controlled trials of ASB screening and/or treatment have established the lack of efficacy in diabetic women, patients with spinal cord injury, catheterized patients, and older adults.² In randomized, controlled trials including patients with spinal cord injury, rates of symptomatic urinary infection and recurrence of bacteriuria were similar in patients receiving antibiotics and those who did not.⁵⁸⁻⁵⁹ Antibiotic treatment in catheterized patients did not decrease symptomatic episodes and increased emergence of more resistant organisms.²

Patient groups in which ASB is particularly hard to diagnose

Nursing home patients—Clinical trials in elderly nursing home residents have consistently found no benefits with treatment of asymptomatic bacteriuria.⁴⁶ The minimum clinical criteria to initiate antimicrobial therapy in the general nursing home population were established in 2001.⁶⁰ Despite extensive research demonstrating a lack of benefit and a potential for harm for antibiotic use for ASB, nursing home residents frequently receive an antibiotic for ASB. In a recent study investigating antibiotic use among residents in four nursing homes, half of the antibiotic prescriptions were for residents with no documented

UTI symptoms.⁴³ In another study, only 11% of suspected UTI episodes in nursing home residents with advanced dementia had both the symptoms and laboratory criteria necessary for diagnosis of UTI; 82 (75%) of the 110 episodes that did not meet the minimum criteria for treatment were treated with antimicrobials.⁶¹ The usefulness of urinary specimens in diagnosing UTI was questionable, because the proportion of episodes with a positive urinalysis and culture was similar for those that met (83%) and did not meet (78%) minimum clinical criteria ($P=0.06$).⁶¹

Intensive Care Unit (ICU) patients—ICU patients and older institutionalized patients have in common a limited ability to communicate. Most patients who are hospitalized in ICUs receive an indwelling urinary catheter to monitor urine output; many are also on ventilators and have centrally-placed vascular catheters. Thus, determining the source of fever in an ICU patient with an indwelling catheter is particularly difficult, particularly as catheter-associated bacteriuria is so common. A study in a French ICU of two different urinary catheter types found that 9.6% of patients developed bacteriuria on day 12 ± 7 , although these study catheters had been placed under ideal conditions.⁶² In a trauma ICU study in 510 patients, the tendency to blame fever on bacteriuria was not supported by evidence. Although there was a significant association between having a urine culture and having a fever ($P<0.001$), bacteriuria was not associated with fever, leukocytosis, or the combination of fever and leukocytosis.⁶³ A systematic review and meta-analysis of 11 studies in adult ICU patients with catheter-associated bacteriuria (with or without symptoms of CAUTI) found that bacteriuria was associated with increased mortality in unadjusted analysis. However, after restricting the analysis to studies that adjusted for other outcome predictors, bacteriuria was no longer associated with mortality but was possibly related to a small increase in length of stay (mean difference +2.6 days; 95% CI 2.3-3.0).⁶⁴ This finding is in accord with the results of a randomized clinical trial in 60 patients on ICUs who were asymptomatic and catheterized with positive urine cultures.⁶⁵ Treatment of the bacteriuria with antibiotics and catheter exchange did not reduce the rate of urosepsis, bacteremia, or positive urine cultures on day 15 after enrolment.

Patient groups with ASB and inadequate evidence to guide management

Evidence to guide management of preoperative ASB before nonurologic procedures is limited. A recent study addressed whether preoperative screening for and treatment of ASB in patients undergoing cardiovascular, orthopedic, or vascular procedures confers benefits.⁶⁶ Among patients with a preoperative culture, patients with bacteriuria and those without bacteriuria were compared for postoperative complications. Surgical site infection was similarly frequent among patients with bacteriuria versus those without, while postoperative UTI was more frequent among patients with bacteriuria (9% vs. 2%, $P=0.01$). Among the 54 patients with a positive screening culture, a greater proportion of treated patients developed a surgical site infection compared to untreated patients (45% vs. 14%, $P=0.03$). However, the findings from this small observational study should be interpreted with caution because of the high likelihood of confounding factors.

Few studies have evaluated the impact of bacteriuria in patients undergoing major joint replacement surgery.⁶⁷ The majority of these studies had retrospective design and were published over a decade ago.⁶⁷ In one prospective study of hip and knee arthroplasty, preoperative bacteriuria was not associated with subsequent joint infection at one year after the procedure.⁶⁸ However, all patients in this study had received preoperative cefuroxime therapy. In a recent prospective randomized study including 471 patients, ASB occurred in 8 (3.5%) of 228 patients undergoing total hip arthroplasty and in 38 (15.6%) of 243 patients undergoing hemiarthroplasty.⁶⁹ Patients were randomized to receive specific antibiotic treatment or no treatment. No case of prosthetic joint infection from urinary origin was

identified in any study group in this trial. However, the sample size might have been too small to detect an effect in this trial. Whether screening for and treating bacteriuria prior to prosthetic joint implantation confers any clinical benefit is unknown.

Another area lacking definitive evidence in the IDSA guidelines how to manage existing bacteriuria at the time of removal of a urinary catheter. Since publication of the guidelines, additional literature on this topic provided enough data to perform a meta-analysis.⁷⁰⁻⁷² In a systematic review and meta-analysis of pooled data from seven studies, antibiotic prophylaxis was beneficial with an absolute reduction in risk symptomatic UTI of 5.8% between intervention and control groups and a risk ratio of 0.45 (95% 0.28 to 0.72).⁷³ One obvious practical consideration is that to implement this approach, testing of urine prior to catheter removal would need to be performed in time to have urine culture results at catheter removal or shortly thereafter.

Prevention of inappropriate treatment of ASB

Several interventional studies have addressed the issue of inappropriate treatment of ASB (Table 2).⁷⁴⁻⁸⁰ These guidelines implementation interventions were heterogeneous and measured different outcomes. However, all strategies went beyond passive education, many incorporating audit and feedback or interactive learning, and all reported a decrease in antibiotic use. One common theme of these diverse and successful strategies is that they engendered medical mindfulness, or making a thoughtful clinical decision, rather than reflexive use of antibiotics.⁸¹⁻⁸² Our ongoing intervention, entitled “Kicking CAUTI: the No Knee-Jerk Antibiotics Campaign,” encourages clinicians to stop and think before ordering cultures and prescribing antibiotics for catheter-associated bacteriuria.⁸³ The two main tools used in the intervention are (1) an evidence based, actionable algorithm that distills the guidelines into a streamlined clinical pathway and encourages a mindful pause (Figure 1),⁹ and (2) case-based audit and feedback to train clinicians to use the algorithm. This algorithm was developed with input from the authors of the IDSA ASB and CAUTI guidelines, and use of this algorithm improved non-experts diagnostic accuracy of ASB versus CAUTI when applied retrospectively to actual cases.⁹ Overall, these interventional studies offer hope that guidelines implementation can decrease antimicrobial overuse for ASB. The design of interventions to reduce overutilization for ASB should integrate behavioral theory so that the underlying cognitive, behavioral, and financial drivers are addressed.⁸⁴ Interventions should be tailored to fit specific goals and also need to address the root causes of inappropriate prescribing.⁸⁵

Summary

The most important and far-reaching consequences of ASB are not the impact of this condition per se on the individual patient but the negative consequences of overtreatment of ASB in terms of antimicrobial resistance, suprainfections, and unnecessary costs. Increasing awareness that ASB usually does not require treatment led to eliminating ASB from infection control surveillance programs, but this change in surveillance definitions will not in itself change clinical practice.⁸⁶ Likewise, although the epidemic of overtreatment of ASB has been thoroughly documented, these descriptions in themselves will not lead to a solution unless their data serve as a foundation for interventions to optimize management of ASB. Unfortunately, awareness that overtreatment of ASB is a problem has preceded any immediate widespread solutions; currently many of the episodes diagnosed and treated as CAUTI in the hospital are really ASB.^{20,44,87} In the future, perhaps some of the resources that have been channeled into reducing CAUTI and other healthcare-associated infections⁸⁸ can be used to support effective ASB guidelines implementation programs.

Review criteria

We developed a search strategy that covers the main subject area of the review (asymptomatic bacteriuria) and performed systematic literature search in the Medline database. The search was limited to articles published in English between 2002–2013. We searched initially using the following search strategy: “Asymptomatic bacteriuria AND (Anti-bacterial agents OR antimicrobial OR antimicrobials OR anti-microbial OR antimicrobials OR antibiotic OR antibiotics OR anti-bacterial OR antibacterial OR antibacterials).”

We used the following abstract appraisal criteria:

- Title or abstract addresses one or more of the study questions
- Title or abstract identifies primary research or systematically conducted secondary research

We also searched reference lists of retrieved articles (particularly older literature) and hand searched abstracts from key journals. We used additional search strategies for each subtopic, including the following search terms “catheter-associated urinary tract infection,” “bacteriuria and diabetes,” “bacteriuria and non-pregnant,” “bacteriuria and spinal cord injury,” “bacteriuria and intensive care OR ICU OR critically ill,” “bacteriuria in elderly,” “bacteriuria and nursing home,” “antibiotic overuse,” “performance measures,” “*Escherichia coli* and bacteriuria,” “bacteriuria and pregnancy,” “bacteriuria and preoperative,” “bacteriuria and urinary catheter removal,” “*Escherichia coli*,” and “bacteriuria and anti-bacterial agents,” among others.

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Box 1**Risk Factors for bacteriuria in general²¹**

Sexual activity*
Use of diaphragm with spermicide*
Older age
Female sex
Diabetes mellitus
Neurogenic bladder
Hemodialysis
Urinary retention
Urinary catheter use
 Indwelling
 Intermittent
 External (condom)

*In sexually active, non-pregnant women ages 18-40.²⁹

Key points

- Asymptomatic bacteriuria (ASB) is defined by the presence of bacteria in an uncontaminated urine sample collected from a patient without signs or symptoms referable to the urinary tract.
- ASB is distinguished from symptomatic UTI by the absence of signs and symptoms of UTI or by determination that a nonurinary etiology accounts for the patient's symptoms.
- ABU is a very common condition in diverse patient groups.
- Overtreatment of ASB with antibiotics is also very common, particularly in patients who are hospitalized, have urinary catheters, or live in a nursing home setting.
- Unnecessary antimicrobial treatment of ASB confers harm to the individual and to society.

Catheter-Associated UTI (CAUTI) vs Asymptomatic Bacteriuria

(Patient with urinary catheter or catheter use within 48 hours)

Figure 1.

Validated algorithm to assist in clinical decision making about positive urine cultures in catheterized patients. The focus of the algorithm is on reminding the clinician to stop and think about two key questions before reflexively prescribing antibiotics for bacteriuria. Reprinted here with permission from BioMed Central.⁹

Table 1
Studies documenting widespread inappropriate use of antibiotics for ASB

Reference	Country	Study design	Study population	Findings
Hecker <i>et al.</i> ⁸⁹ (2003)	USA	Prospective, observation over 14 days	129 inpatients	99 of 576 (17%) unnecessary days of antibiotics were for ABU
Dalen <i>et al.</i> ⁹⁰ (2005)	Canada	Prospective, observation over 26 days	29 inpatients with urinary catheters, positive urine cultures and no symptoms of UTI	15 (52%) were prescribed unnecessary antimicrobials
Cope <i>et al.</i> ¹⁹ (2009)	USA	Retrospective review over 3 months	197 inpatients with urinary catheters and positive urine cultures	Of 169 treated episodes of bacteriuria 53 (31%) were ASB
Gandhi <i>et al.</i> ⁹¹ (2009)	USA	Retrospective review over 3 months	414 inpatients	Of 49 patients who were treated for UTI, 13 (26%) had ASB
Silver <i>et al.</i> ⁶ (2009)	Canada	Prospective, observation over 1 year	137 inpatients with positive urine cultures	43 (64%) patients with ASB were treated
Khawcharoenporn <i>et al.</i> ⁴² (2011)	USA	Retrospective review over 8 months	676 emergency department patients with positive urine cultures	37 (20%) of 184 patients with ASB were treated with antibiotics
Werner <i>et al.</i> ⁸⁷ (2011)	USA	Prospective, observation over 6 weeks	226 inpatients who received fluoroquinolones	Of 690 days of unnecessary fluoroquinolone therapy, 158 (23%) were for ABU
Lin <i>et al.</i> (2012) ²⁰	USA	Retrospective review over 3 months	339 inpatients, outpatients and emergency department patients with enterococcal bacteriuria	60 (32.8%) of 183 episodes of ASB inappropriately treated with antibiotics
Philips <i>et al.</i> (2012) ⁴³	USA	Retrospective review over 6 months	16 catheterized nursing home patients	19 (83%) of 23 treated episodes were asymptomatic
Chiu <i>et al.</i> (2013) ⁴⁴	Canada	Retrospective review over 6 months.	80 inpatients with indwelling urinary catheters	23 (58%) of 40 patients with a positive culture result were prescribed unnecessary antimicrobials
D'Agata <i>et al.</i> (2013) ⁶¹	USA	Prospective over 12 months	72 nursing home residents with dementia	82 (75%) of 110 episodes of suspected UTI were prescribed unnecessary antibiotics
Heintz <i>et al.</i> (2013) ⁴⁵	USA	Retrospective review over 3 years	252 patients with vancomycin-resistant enterococci in urine	33 (21.3%) of 155 asymptomatic patients were treated

Abbreviations: ASB asymptomatic bacteriuria. USA: United States of America

Table 2
Interventional Studies to Decrease ASB Overtreatment

Reference	Study setting	Study design	Intervention	Outcomes
Loeb <i>et al.</i> ⁷⁴ (2005)	Nursing homes	Cluster randomized controlled trial	Multifaceted, algorithm use taught by case scenarios in interactive sessions	Fewer courses of antimicrobials for suspected UTI in intervention homes (1.17/1000 resident days) than in control homes (1.59/1000 resident days)
Bonnal <i>et al.</i> ⁷⁵ (2008)	University-affiliated geriatric hospital	Audit before and after intervention	Pocket card plus post-prescription audit and feedback for positive urine cultures managed inappropriately	Antibiotic use for ASB decreased from 196 days during the pre-intervention year to 150 days during the intervention year, $P = 0.007$
Zabarsky <i>et al.</i> ⁷⁸ (2008)	Veterans Affairs long-term care facility	Audit before and after intervention	Pocket cards, educational sessions, audit and feedback	Decrease in urine cultures sent, reduction in treatment of ASB and in total days of antimicrobial therapy (from 168 to 117 per 1000 patient-days, $P < 0.001$)
Pavese <i>et al.</i> ⁷⁹ (2009)	University-affiliated hospital	Controlled audit before and after intervention	Distribution of guidelines and report plus a 1 hour interactive educational session	Antibiotic use for ASB in intervention group decreased from 74% before intervention to 17% afterwards ($P = 0.01$)
Linares <i>et al.</i> ⁸⁰ (2011)	Veterans Affairs hospital	Audit before and after intervention	Memorandum placed in electronic medical record if antibiotics were inappropriate	Mean duration of treatment of ASB decreased from 6.3 days in control group to 2.2 days in intervention group ($P < 0.001$)
Egger <i>et al.</i> (2013) ⁷⁶	Teaching hospital	Before and after	Multifaceted, implementation of guidelines, catheter reminders, and internet-based teaching cases	ASB treatment dropped significantly from 22 to 10 treatment days per 1,000 patient days (incidence rate ratio 0.46, 95% CI 0.33-0.63)
Pettersson <i>et al.</i> (2011) ⁷⁷	Nursing homes	Cluster randomized controlled trial	Education about UTI with feedback on baseline antibiotic prescription data	The proportion of overall infections treated with an antibiotic decreased significantly by -0.124 (95% CI -0.228, -0.019) compared with the control group

Abbreviations: ASB, asymptomatic bacteriuria; UTI, urinary tract infection