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Infectious Disease

Asymptomatic Bacteriuria: To Treat or Not to Treat

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Urinary tract infections (UTIs) are a frequent diagnosis in older adults, leading to substantial antimicrobial use. Increased antimicrobial use is associated with higher rates of resistance, making future infections more difficult to treat. Unfortunately, many UTIs actually represent asymptomatic bacteriuria, which should not be treated in most cases. Adhering to clinical guidelines (based on high-quality evidence from randomized trials) would likely result in fewer UTI diagnoses, less antimicrobial use, and decreased antimicrobial resistance. Knowing when treatment for asymptomatic bacteriuria is recommended, and limiting therapy to these well defined circumstances is vital to appropriately managing a patient with a positive urine culture.

Key words: *urinary tract infection, asymptomatic bacteriuria, catheter-associated bacteriuria, antimicrobial management*

Introduction

A positive urine culture (UC) obtained from a patient who presents with symptoms consistent with a urinary tract infection (UTI) presents little management difficulty. Antimicrobial therapy is indicated for both cystitis (to hasten symptom resolution) and pyelonephritis (to hasten resolution and to prevent progression to severe sepsis). All that remains is to administer an effective antimicrobial for a reasonable duration. However, when urine has been obtained from an asymptomatic patient, a positive UC is not necessarily an indication for therapy. Indeed, treating asymptomatic bacteriuria (ABU) is recommended in only a few narrowly defined circumstances; in the great majority of cases, antimicrobials should be avoided, both to prevent adverse drug effects and to limit the development of resistance. However, despite randomized trials demonstrating no benefit, patients with ABU often receive antimicrobials. This article reviews the evidence against treating ABU, highlights the select circumstances in which ABU does warrant therapy, and explores situations in which uncertainty can arise. Details on the treatment of symptomatic UTI are not discussed; readers are referred to other reviews.[1,2]

Definitions

A positive UC is variably defined, but in the setting of symptoms, signs, or findings possibly indicating a clinically significant UTI (Table 1), any microbial growth is significant.[3–5] Without clinical evidence of a UTI, a positive UC (i.e., ABU) refers to the isolation of $\geq 10^5$ colony-forming units (CFU) per millilitre from a voided urine sample, a numerical threshold chosen to exclude false-positives arising from contamination during sample collection or processing. If an aseptically inserted catheter is used to obtain urine, a lower threshold ($\geq 10^2$ CFU/mL) for ABU is sometimes applied. The appropriate threshold for use with urine samples collected via an indwelling catheter is not well defined, but low colony counts ($<10^5$ CFU/mL) may represent organisms arising from colonization of the catheter, not from the bladder, and tend to not be present on repeat testing if a new catheter is placed.[6]

Epidemiology

Symptomatic UTI is common, occurring in 40–50% of women during their lifetime[7] and in 10–15% of men.[8] Asymptomatic bacteriuria is also common, although the prevalence at any single time point is <5% in healthy non–older adults.[9] Certain patient factors markedly increase the prevalence of ABU, including older age, coexisting medical conditions, and the use of urinary catheters (both intermittent and indwelling) (Table 2).[7,9–15]

Treatment of Asymptomatic Bacteriuria

Because ABU is a risk factor for a subsequent symptomatic UTI, numerous clinical trials have tested the hypothesis that antimicrobial therapy for ABU would be beneficial.[13,16–20] Assessed outcomes included symptomatic UTI, mortality, antimicrobial use, adverse drug events, progression to diabetic nephropathy, incontinence, and reinfection with resistant organisms. Older adults were well represented, with the mean (or median) age in five trials being ≥80 years. Although antimicrobial therapy successfully reduced the proportion of subjects with bacteriuria, no clinically relevant benefits were observed. On the contrary, treatment of ABU resulted in increased antimicrobial use, adverse drug effects, and reinfection with resistant organisms. Based on these findings, current Infectious Diseases Society of America guidelines discourage screening for or treating ABU in most patients.[9]

Two specific circumstances are exceptions to the general rule that ABU should not be screened for or treated. The first, of little relevance to geriatricians, is pregnancy. Pregnant women with ABU have a significantly increased risk of developing pyelonephritis, which can be a severe threat to the health of both the mother and fetus.[21] Because antimicrobial therapy greatly reduces the risk of pyelonephritis during pregnancy, screen-

ing and treatment for ABU has become standard prenatal care.[9,21]

The second circumstance in which screening for and treating ABU is beneficial is surgical disruption of the bladder or urethral mucosa. Most evidence for this recommendation comes from studies of transurethral resection of the prostate (TURP). If performed in the setting of bacteriuria, a majority of subjects develop bacteremia, with a smaller (but significant) percentage of subjects developing overt sepsis.[22] Because antimicrobial therapy effectively prevents these complications, screening and treatment for ABU is the standard of care prior to TURP. The timing of therapy is unclear; administration either the night before or the morning of the procedure has been successful in clinical trials.[23,24] Antimicrobials should be chosen based on susceptibility testing of the isolated organism, which is increasingly unpredictable. Therefore, if the clinical microbiology laboratory does not routinely perform identification or susceptibility testing on samples with low-concentration growth ($<10^5$ CFU/mL), it seems prudent to request that this be done to aid in selecting active therapy.

There are few data from which to draw conclusions regarding procedures other than TURP. Guidelines from the American Urological Association primarily address prophylactic antimicrobial therapy, which is often given without obtaining a urine sample and stopped within 24 hours.[25] A reasonable approach may be to obtain a UC prior to any urological procedure in which urothelial bleeding is anticipated, in order to choose a regimen that has activity against the current ABU strain. In most instances, a single perioperative dose of antimicrobial is sufficient, and no more than 24 hours of therapy should be administered unless a urinary catheter is placed. In the latter case, standard practice is to continue antimicrobials until the catheter is removed, although minimal evidence supports this practice.[22,24]

Special Circumstances

Pyuria

The concept that leukocytes (or their surrogate marker leukocyte esterase) in a urinalysis implies a clinically significant infection is widely held. However, in clinical trials evaluating the treatment of ABU, the great majority of bacteriuric patients also had pyuria. No evidence exists to show that the presence of pyuria, at any level, identifies a subset of patients with ABU who will benefit from antimicrobial therapy. Pyuria is expected with bacteriuria and should not factor into the decision regarding whether to treat the patient.

Preoperative Evaluation

Practitioners involved in preoperative evaluations often encounter a situation in which a referring surgeon requires a urinalysis or culture prior to operating, with the implicit expectation that abnormal results should be addressed prior to surgery. Evidence supporting this practice outside of urological procedures is scarce. One study of subjects undergoing knee surgery found that preoperative urinalyses were frequently abnormal, most because of pyuria. These abnormalities were inconsistently attended to, with no differences in postoperative wound infection observed between patients who received antimicrobials and those who did not.[26] Because of the rarity of postoperative wound infections caused by a urinary source, the cost-to-benefit ratio of preoperative urine testing is prohibitive, with an estimated US$1.5 million needed to prevent a single wound infection,[27] despite the relatively low cost of an individual test. Because of the lack of benefit, the potential for harm, and the large aggregate costs, preoperative screening for UTIs should be avoided unless the planned procedure is likely to cause urothelial bleeding.

Renal Transplantation

Recipients of renal allografts are at a higher risk for UTIs because of their surgically altered urinary tract, immune suppression, and, often, underlying disease that may predispose to UTIs, such as diabetes, polycystic kidney disease, and others. Because of the high incidence of UTIs and gram-negative bacteremia in the post-transplantation period, most transplant centres use prophylactic antimicrobials to prevent UTIs in the immediate post-transplantation period, often for 6 months. This approach leads to a decrease in symptomatic UTI, bacteremia, and other bacterial infections.[28] Beyond 6 months after transplantation, UTI diagnoses are associated with increased mortality[29]; however, treatment (either by continuing prophylaxis or by screening for and treating ABU) is an unproven strategy that cannot be recommended.

Table 1: Symptoms, Signs, and Findings Possibly Consistent with Symptomatic Urinary Tract Infection*

Category	Specific Symptom or Finding
Symptom	Dysuria
	Frequency
	Urgency
	Fever (reported)
	New or worse incontinence
	Suprapubic pain
	Abdominal pain
	Flank pain
	Lethargy or weakness
	Otherwise unexplained delirium
Examination findings	Fever (measured)
	Abdominal pain
	Costovertebral angle or flank tenderness
Laboratory result	Elevated peripheral leukocyte count

*Based on published data and anecdotal evidence.

Table 2: Prevalence of Asymptomatic Bacteriuria in Selected Populations

Population	Prevalence (%)	Reference No.
Older adults, community living*		
Women	18, 19	10, 11
Men	6	10, 11
Older adults, living in long-term care facility		
Women	25–47	12, 14
Men	30–33	12, 13
Patients using intermittent catheterization	61	15
Patients with indwelling catheters		
Short-term†	10–30	30
Long-term‡	100	30

*Older adults were defined as ≥68 in one study and ≥80 in another.
†Defined as 2–4 days.
‡Defined as ≥30 days.

Patients with Indwelling Catheters

Among patients with indwelling urinary catheters, both suprapubic and urethral, the urinary tract becomes colonized at a predictable rate of 3–10% per day, such that by 30 days of catheter use, bacteriuria is almost universal.[30] Similar to patients without an indwelling catheter, if no manifestation of infection is present, urine should not be cultured. Because typical UTI symptoms of dysuria, frequency, and urgency are unreliable with a catheter in place, clinicians should look for alternative manifestations of UTI. These include fever, leukocytosis, malaise, and abdominal discomfort. Because these are nonspecific symptoms and findings, a thorough history and physical examination should be performed to evaluate for other potential causes. If no other explanation is found for the observed clinical deterioration, obtaining a UC, treating for presumptive UTI, and assessing the response to therapy is appropriate.

Removing an indwelling catheter in the presence of bacteriuria is associated with both high rates of persisting bacteriuria and of subsequent symptomatic UTI. Antimicrobial therapy at the time of catheter removal is protective against symptomatic UTI, even when given as a single dose.[31] However, because a significant proportion of subjects with post-catheterization ABU will clear their bacteriuria spontaneously, current guidelines suggest considering antimicrobial therapy to prevent symptomatic UTI only if a UC remains positive 48 hours after catheter removal.[9] Whether the costs, inconvenience, and unnecessary antimicrobial use of routinely screening for persistent post-catheterization ABU and treating it when found are outweighed by the resulting clinical benefits remains undefined.

Patients with Decreased Sensory or Cognitive Function

Patients with impaired sensation or reporting ability present a special challenge with respect to assessment for clinically significant UTI. Such patients include those with spinal cord injuries, multiple sclerosis, cerebrovascular disease, dementia, and other neurological disorders. Their deficits often reduce the sensitivity of typical UTI symptoms such as dysuria, and some have coexisting bladder emptying problems, often managed with a urinary catheter, predisposing to persistent ABU. Finally, many noxious stimuli, including infection, manifest as nonspecific findings, including increased autonomic instability, malaise, and spasticity. Because of a lack of high-quality evidence, providers must rely on experience and patient-specific factors when differentiating a non-UTI process (occurring in a patient with chronic ABU) from a symptomatic UTI.[32] As recommended for patients with an indwelling catheter, a thorough search for other causes should be undertaken. If no other cause of the clinical deterioration is found and the clinical manifestations are sufficiently consistent and concerning as to warrant medical intervention (with its attendant hazards), a UC should be obtained and treatment for UTI initiated.

Staphylococcus aureus Bacteriuria

Because *Staphylococcus aureus* bacteriuria has been documented in patients who were subsequently found to be bacteremic, the relationship between *S. aureus* bacteriuria and subsequent invasive infection has been investigated. In a longitudinal cohort study of 102 older men with *S. aureus* bacteriuria (one-third symptomatic and two-thirds asymptomatic), individuals with persistent ABU

Key Points

- Asymptomatic bacteriuria increases with age, catheter use, and in institutions.
- In most cases, antimicrobial therapy for asymptomatic bacteriuria is unnecessary.
- Asymptomatic bacteriuria should be treated prior to urological surgery with anticipated bleeding into the urinary tract.
- Long-term indwelling urinary catheters are universally colonized with bacteria.
- Symptoms, not laboratory tests, should drive antimicrobial therapy.

Clinical Pearls

The level of pyuria (even when reported as "too numerous to count" or "clumps") is irrelevant in a patient without symptoms or signs of a urinary tract infection (UTI).

Asking the microbiology laboratory to fully work up an organism can provide valuable information and aid treatment in a patient with low-concentration bacterial growth and symptoms consistent with a UTI.

had a high rate (34%) of subsequent clinically significant *S. aureus* infections, including eight cases of bacteremia (57% of the subsequent infections).[33] Pulsed-field gel electrophoresis results suggested that the subsequent infections were caused by strains identical or closely related to the initial urine isolate. Although these data suggest that *S. aureus* bacteriuria is associated with a high risk of subsequent serious infection and might be interpreted as implying that eradication may be beneficial, it should be remembered that an analogous situation occurred with ABU in diabetic patients. In that clinical context, subsequent trials proved that antimicrobials not only provided no benefit but also caused documented direct harm to subjects.[18] Until more studies evaluate the efficacy of treating *S. aureus* ABU, treatment with antimicrobials cannot be recommended. Clinicians should be aware of the possibly increased risk of subsequent staphylococcal infections in such patients, and evaluate any change in clinical status accordingly.

Conclusion

With few exceptions, only patients with a symptomatic UTI should receive antimicrobials for bacteriuria. It is vital to keep the high population prevalence of ABU in mind when treating older adults, especially in settings such as long-term care facilities, where nearly every second resident can be expected to have ABU. Treating all persons with ABU would result in enormous antimicrobial use, increased costs, antimicrobial resistance, and harm to patients. Clinicians should work with their institutions and nursing staff to ensure that a UC is obtained only when signs of a UTI are present, or in the setting of a planned invasive urological procedure or pregnancy.

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