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## URINE CULTURES IN ACUTE PYELONEPHRITIS: KNOWING WHAT YOU ARE UP AGAINST

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### Editor's Note:

Urine cultures can provide information on the microbiological cause and optimal treatment for patients diagnosed with acute pyelonephritis, but the need for routine cultures for patients with simple, uncomplicated pyelonephritis is unclear. In this Clinical Controversies series our pro and con discussants present opposing viewpoints of the benefits and drawbacks of routine urine cultures among patients with simple, uncomplicated pyelonephritis.

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In the United States, annual rates of acute pyelonephritis in adults approach 15 to 17 cases per 10,000 women and 3 to 4 cases per 10,000 men, the majority of which are treated in ambulatory settings such as the emergency department (ED).<sup>1</sup> Urinary pathogen identification through microbiologic culture and in vitro antibiotic susceptibility testing optimizes diagnosis and management of acute pyelonephritis and is supported by international clinical practice guidelines.<sup>2</sup> A properly collected, noncontaminated urine culture provides meaningful and objective data not only to guide antibiotic therapy for the patient but also to track regional antibiotic resistance rates.

Urinary pathogen identification in the context of acute pyelonephritis aids the delivery of patient-centered care. When a causative microorganism is isolated, urine culture confirms the presence of a bacterial infection, identifies potential pharmacologic treatment options, and establishes the basis for tailoring antibiotic therapy to a unique episode of infection. Because microbiologic culture results may not be available for 48 to 72 hours, most ED antibiotic regimens directed against acute pyelonephritis are empiric. Selecting a safe empiric antibiotic to treat acute pyelonephritis can be challenging. Increasing antibiotic resistance rates are a serious problem in ED patient populations.<sup>3–6</sup> Greater than 20% of urinary *Escherichia coli* isolates are now resistant to trimethoprim-sulfamethoxazole.<sup>7</sup> Between 2003 and 2012, ciprofloxacin resistance increased from 4% to 12%; in the elderly, ciprofloxacin resistance is nearly 30%.<sup>7</sup> Furthermore, infections caused by extended-spectrum  $\beta$ -lactamase-producing Enterobacteriaceae (ESBL) are an underrecognized but important cause of acute pyelonephritis in the ED, even in community settings.<sup>4,5</sup> Advancing age, a history of recurrent or resistant urinary tract infection, recent antibiotic or other health care–related exposure, and various medical comorbidities are associated with a greater risk

of acute pyelonephritis caused by an antibiotic-resistant organism.<sup>3,4,8</sup> Yet a surprising number of ED patients with ESBL infections lack these traditional risk factors.<sup>5</sup>

Blindly selecting empiric antibiotics without follow-up culture data places patients at a real risk of adverse events. Individuals treated with an empiric antibiotic without activity against a urinary pathogen (pathogen-drug mismatch) identified in culture are more likely to have persistence or relapse of infection, often requiring additional care, including return ED visits.<sup>6,8,9</sup> Earlier discovery of pathogen-drug mismatch followed by revision of an inadequate antibiotic regimen can only enhance and expedite treatment success. In integrated health care settings in which timely ambulatory follow-up is ensured, treatment of acute pyelonephritis with a narrow-spectrum oral antibiotic (eg, trimethoprim-sulfamethoxazole, a  $\beta$ -lactam) with close monitoring of the patient and urine culture results could be considered. The advantages of this approach include avoiding the collateral damage of fluoroquinolones (eg, *Clostridium difficile* infection) and reducing selection pressure for future antibiotic-resistant organisms. Obtaining a urine culture in the setting of acute, uncomplicated pyelonephritis promotes targeted, patient-focused care.

Antibiograms for urinary pathogens including *E coli* are only as accurate and reliable as the microbiologic culture and antibiotic susceptibility data on which they are built. Sampling bias favoring hospitalized patients with severe infection or selected ambulatory patients with a history of antibiotic-resistant infection can paint a confusing picture when a hospital antibiogram is used to decide empiric therapy for uncomplicated pyelonephritis in the ED. Increasing evidence suggests that ED-specific antibiograms may differ significantly from inpatient antibiograms.<sup>10,11</sup> Antibiograms reflective of the heterogeneous ambulatory population an ED cares for not only increase confidence in empiric ED antibiotic prescribing but also yield important and timely insights into community antibiotic resistance patterns. Obtaining urine cultures for a wide spectrum of patients presenting with acute pyelonephritis ensures an accurate characterization of the constantly evolving epidemiology of urinary tract infections and ultimately helps refine population-based treatment strategies and guidelines.

Although urine cultures may not change management for the majority of ED patients found to have a susceptible urinary pathogen, antibiotic resistance should be a concern for all emergency health care professionals. In a study of 10 academic US EDs participating in the EMERGENCY ID NET, greater than 45% of patients with acute pyelonephritis caused by a fluoroquinolone-resistant pathogen and 75% with ESBL infection initially received an empiric antibiotic lacking in vitro activity.<sup>4</sup> Of patients with ESBL infection who were discharged home from the ED, nearly 78% were prescribed a nonactive oral antibiotic. In an era of increasing antibiotic resistance, urine cultures obtained in the ED can significantly influence downstream antibiotic therapy for these patients.

We acknowledge that there are limitations with urine cultures. Periurethral contamination of urine specimens and inappropriate culturing of patients with abdominal pain from a separate cause can lead to false-positive results, triggering unnecessary antibiotic therapy. Standard urine culture techniques may fail to detect a significant number of fastidious and emerging urinary pathogens in clearly symptomatic patients.<sup>12</sup> Urinary pathogens deemed resistant by in vitro testing may not reveal the entirety of in vivo antibiotic activity. Several antibiotics

achieve significantly higher concentrations in urine compared with serum, increasing their efficacy in treating urinary tract infections.<sup>13</sup> Innovative rapid molecular techniques for urinary pathogen identification and antibiotic susceptibility testing may in time render conventional urine culture obsolete.<sup>14</sup>

The fundamental questions of what urinary pathogen is responsible for a patient's infection and what antibiotic can effectively eradicate it with the least disruption to the human microbiome are worthy of asking if we are to be responsible stewards of increasingly finite antibiotic resources and hope to stem the tide of antibiotic resistance. For now, urine culture continues to provide meaningful answers to these questions.

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