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Laboratory Diagnosis of Urinary Tract Infections: Guidelines, Challenges, and Innovations

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Abstract

The culture-based diagnosis of urinary tract infections (UTIs) present several challenges to clinical microbiologists, physicians, and the health care system in general because the diagnosis of UTI is not always straightforward. The 8 million office visits for the assessment of UTIs each year represent a significant health care cost of approximately $1 billion annually. The resulting 1.5 million hospitalizations further impact the health care system. UTIs represent 40% of nosocomial infections, and they are usually associated with urinary catheters. Importantly, catheter-associated urinary tract infections (CAUTIs) are one of the hospital-acquired complications chosen by the Centers for Medicare and Medicaid Services for which hospitals no longer receive additional payment. Although this rule may result in an increased focus on CAUTIs, increased education for health care workers, early catheter removal, and alternatives to indwelling catheterizations, it may also result in more urine specimens being submitted for culture. An increase in urine cultures will definitely have an impact on both clinical microbiology staffing and laboratory expenditures, especially if the urine cultures are positive for significant amounts of microbial growth. Therefore, it is imperative that the clinical microbiology laboratory employ well-documented guidelines for processing and interpreting urine cultures and implement state-of-the-art methodology, when appropriate. The purpose of this review is to discuss recent guidelines and recommendations for the collection and processing of urine specimens, interpretation of culture results, current challenges, and potential options for routine urine culture.

Introduction

The number of urine specimens submitted for culture usually exceeds that of any other specimen types received in the clinical microbiology laboratory. Specimens submitted from ambulatory sites are usually midstream, voided specimens. Approximately 60% to 70% are culture negative. Of the positive urine cultures showing bacterial growth, approximately 50% contain common uropathogens, primarily *Escherichia coli*, while the remaining cultures showing growth contain multiple organisms or commensal flora. These urine cultures usually present little or no challenge to the clinical microbiologist, unlike specimens collected by invasive methods.

Monitoring of urinary catheters has always been a justification for microbial analysis. However, the recent Centers for Medicare and Medicaid Services (CMS) rule related to nonpayment for nosocomial infections associated with urinary catheters (1) will likely increase the number of positive cultures containing less common, more resistant organisms, triggering increased antibiotic usage. Since these specimens are collected by invasive methods, the clinical microbiologist may be further challenged by being required to work up as few as 1,000 CFU/ml.

Although it is important for the clinical microbiologist to be knowledgeable and proficient in the interpretation and identification of microorganisms, it is also important to understand the clinical manifestation of urinary tract infection (UTI), as well as the significance of the colony count associated with each method of collection.

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Guidelines for Collection, Processing, and Interpretation

Several publications and collaborations have been ongoing for the purpose of developing guidelines to improve standards of practice for physicians and clinical microbiology laboratories. The American Society for Microbiology (ASM) began introducing such guidelines almost 40 years ago with the *Cumitech* (*Cumulative Techniques and Procedures in Clinical Microbiology*) series. The purpose, as stated by the first editorial board, was to provide consensus recommendations by the authors as to appropriate state-of-the-art operating procedures for clinical microbiology laboratories that may lack the capability to fully evaluate routine or new methods (2). They also stated that the procedures were not proposed as "standard" methods. These guidelines were based on routine laboratory practices; however, the focus has shifted to developing evidence-based guidelines. This is reflected in the renaming of the *Cumitech* series to *Practical Guidance for Clinical Microbiology*.

Currently, there is a much better understanding of UTI regarding pathogenesis, epidemiology, and management as a result of several clinical studies involving many different patient populations. These studies have been used as the basis for developing guidelines. A recent collaboration between the Infectious Diseases Society of America (IDSA) and the ASM has resulted in a publication that provides information on which tests are valuable and in which contexts and on tests that add little or no value for diagnostic decisions (3). This guide is intended to help physicians appropriately use laboratory tests for the diagnosis of infectious diseases. Although this document addresses several specimen types, guidelines for UTIs are included. Additionally, IDSA has developed guidelines that specifically address UTIs.

Prior to the IDSA and ASM guidelines, clinical microbiologists recognized the need for consensus recommendations for the laboratory diagnosis of UTIs, resulting in the publication of ASM's *Cumitech* 2 series (3). The first *Cumitech* 2 was published in 1975, followed by three subsequent editions, 2A, 2B, and 2C, each about a decade apart. The current *Cumitech* 2C is widely used in the diagnostic microbiology laboratory (4). The document includes valuable information on urine specimen collection and transport, processing and interpretation, result reporting, antimicrobial susceptibility testing, and alternatives to the standard plate culture method.

Urine specimen collection, storage, and transport are critical steps to ensure the quality of the specimen submitted for culture. A recent publication by Kubik and McCarter (5) described the many collection methods, as well as the commercially available urine transport systems. Despite its importance, there is ongoing controversy regarding how urine should be collected and transported to the laboratory. The collaborative IDSA and ASM panel of experts agreed that one of the key points for the laboratory diagnosis of UTI is that urine should not sit at room temperature for more than 30 minutes but should be stored at refrigerator temperatures (2°C to 10°C) if not cultured within 30 minutes. Although the Clinical and Laboratory Standards Institute has not published a specific guideline or standard for the laboratory diagnosis of UTI, transport is addressed in their urinalysis guideline, which states that specimens that cannot be transported immediately to the laboratory, are unable to be refrigerated if immediate transport is not possible, or do not have a bacteriostatic preservative may undergo bacterial overgrowth, leading to falsely elevated colony counts (6). Urine specimens that are improperly collected, stored, and/or transported to the laboratory will often yield inaccurate and misleading culture results, which ultimately may have an adverse impact on the care of the patient.

Contaminated urine specimens are also a challenge for the clinical microbiology laboratory, especially since these cultures often may contain multiple organisms and require more time and expertise than a true positive culture. The most important challenge laboratories face is finding effective methods to educate health care workers and patients regarding the performance of appropriate urine specimen collection. Although urine contamination may not be completely avoidable, it has been reported that providing clear patient instructions on proper specimen collection, followed by specimen refrigeration, is associated with lower contamination rates (7).

The definition of significant bacteriuria varies based on clinical manifestations and methods of collection. For example, cystitis, prostatitis, and urethritis are classified as lower UTIs. Most cases of cystitis have colony counts of $\geq 10^5$ CFU/ml, whereas significant colony counts for prostatitis and urethritis are $\geq 10^3$ and $\geq 10^2$, respectively (8-11). Burd and Kehl (12) reviewed several published practice guidelines for diagnosis and treatment of uncomplicated UTI and agreed that cultures are not needed in most cases of initial uncomplicated cystitis but should be performed for all cases of upper and complicated UTIs . It would be difficult for the laboratory to implement these recommendations without consensus policies across the health care disciplines, evidence-based practice guidelines, and approval from local medical executive committees.

Based upon the definition of significant bacteriuria in different patient populations, several guidelines have been developed. It is important that the most current published documents be used to guide the workup of urine cultures. Older versions of guidelines may be inconsistent with current recommended practices. For example, the first *Cumitech* document, *Cumitech* 2, states that if the colony count is between 10^4 and 10^5 CFU/ml, only one organism should be identified. Identification of two probable pathogens was recommended if the colony count was $\geq 10^5$ CFU/ml for each isolate (2). With each subsequent *Cumitech* edition, culture interpretation was expanded. This was due, in part, to the introduction of several new media and culture systems, rapid manual and automated methods, and the recognition that rare and unusual organisms can cause UTIs, as well as a better understanding of what should be identified based upon clinical considerations.

Inconsistencies among the guidelines created by different processes and organizations can cause confusion and challenges for the clinical microbiology laboratory and physicians. For example, the IDSA guideline for asymptomatic bacteriuria, published in 2005, stated that significant bacteriuria in women was defined as two consecutive voided urine specimens with the isolation of the same