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IDSA GUIDELINES

2024 Clinical Practice Guideline Update by the Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Utility of Blood Cultures in Adults, Children, and Pregnant People

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This paper is part of a clinical practice guideline update on the risk assessment, diagnostic imaging, and microbiological evaluation of complicated intra-abdominal infections in adults, children, and pregnant people, developed by the Infectious Diseases Society of America. In this paper, the panel provides recommendations for obtaining blood cultures in patients with known or suspected intra-abdominal infection. The panel's recommendations are based upon evidence derived from systematic literature reviews and adhere to a standardized methodology for rating the certainty of evidence and strength of recommendation according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach.

Key words. intra-abdominal infection; blood culture; guideline

In adults and children with known or suspected intra-abdominal infection (uncomplicated or complicated), should blood cultures be obtained to effect a meaningful change in antimicrobial therapy?

Recommendation: In adults and children with suspected intra-abdominal infections who have an elevated temperature AND: hypotension and/or tachypnea and/or delirium, OR there is concern for antibiotic-resistant organisms that would inform the treatment regimen, the panel suggests obtaining blood cultures *(conditional recommendation, very low certainty of evidence)*.

Remarks:

- Direct evidence on obtaining blood cultures in patients with intra-abdominal infections is lacking.
- Concern for antibiotic-resistant organisms includes high rates of regional resistance to commonly used agents administered as empiric treatment for intra-abdominal infections, patient history of any colonization or infection with organisms not susceptible to commonly used empiric regimens within the previous 90 days, antibiotic treatment

within the previous 90 days, elderly or immunocompromised patients or patients with other significant comorbidities, and/or healthcare-associated infection.

Recommendation: In non-immunocompromised adults and children with suspected intra-abdominal infections who have a normal/elevated temperature but do not have hypotension, tachypnea, or delirium, and there is no concern for antibiotic-resistant organisms that would inform the treatment regimen, the panel suggests not routinely obtaining blood cultures *(conditional recommendation, very low certainty of evidence for adults/low certainty of evidence for children)*.

Remarks:

- Direct evidence on obtaining blood cultures in patients with intra-abdominal infections is lacking.
- Clinicians should use their best judgment considering the benefits and risks of performing blood cultures. In select cases (e.g., concern for antibiotic-resistant organisms, concern for ascending cholangitis, complex intra-abdominal abscess), blood cultures may be helpful to assist with clinical decision-making and further management. Concern for antibiotic-resistant organisms includes high rates of regional resistance to commonly used agents administered as empiric treatment for intra-abdominal infections, patient history of any colonization or infection with organisms not susceptible to commonly used empiric regimens within the previous 90 days, antibiotic treatment within the previous 90 days, elderly or immunocompromised patients or patients with other significant comorbidities, and/or healthcare-associated infection.

INTRODUCTION

This paper is part of a clinical practice guideline update on the risk assessment, diagnostic imaging, and microbiological evaluation of complicated intra-abdominal infections in adults, children, and pregnant people, developed by the Infectious Diseases Society of America [1-7]. Here, the guideline panel provides recommendations for obtaining blood cultures in adults and children with suspected or confirmed intra-abdominal infection. These recommendations replace previous statements in the last iteration of this guideline [8].

A complicated intra-abdominal infection extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis; this term is not meant to describe the infection's severity or anatomy. An uncomplicated intra-abdominal infection involves intramural inflammation of the gastrointestinal tract and has a substantial probability of progressing to complicated infection if not adequately treated.

These recommendations are intended for use by healthcare professionals who care for patients with suspected intra-abdominal infections.

METHODS

The panel's recommendations are based upon evidence derived from systematic literature reviews and adhere to a standardized methodology for rating the certainty of evidence and strength of recommendation according to the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach (Supplementary Figure 1) [9]. The recommendations have been endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), the American Society for Microbiology (ASM), and the Pediatric Infectious Diseases Society (PIDS). Strong recommendations are made when the recommended course of action would apply to most people with few exceptions. Conditional recommendations are made when the suggested course of action would apply to the majority of people with many exceptions and shared decision-making is important.

A comprehensive literature search (through October 2022) was conducted as part of a systematic review. Key eligibility criteria at both the topic and clinical question levels guided the search and selection of studies. For the clinical questions addressed here, patients admitted to the hospital or emergency department who received a blood culture for any reason were considered, as long as some subset of patients had abdominal involvement. Studies including patients with spontaneous bacterial peritonitis or cirrhosis were excluded. The search was limited to include any randomized controlled trials (no publication date limit) or observational studies published in 2005 or thereafter. Refer to the full list of eligibility criteria in the Supplementary Material.

Included studies underwent critical appraisal according to the GRADE approach, and then an assessment of benefits and harms of care options informed the recommendation(s) [9,10]. Details of the systematic review and guideline development processes are available in the Supplementary Material.

Summary of Evidence

A comprehensive search identified seven studies addressing the panel's prioritized outcomes-change in antimicrobial therapy based on blood culture results and prediction of mortality [11-17]. Only two studies were exclusive to patients with intra-abdominal infection [16,17] (Supplementary Table 1).

Four cohort studies examined how often culture results prompted a change in antimicrobial therapy or clinical management in adults admitted to the hospital who had a blood culture drawn in the emergency department, [11-13,15] and one cohort study examined the same outcomes in children who had a blood culture drawn in the emergency department [17]. Combined data for 8,750 blood cultures obtained from adults demonstrated that cultures were positive in 12.7% of cases (n=1,076). Of these, only 63.9% (n=687) were true positives (i.e., not contaminated cultures), as defined by the respective investigators. The weighted proportion of true positive culture results that drove a change in antimicrobial management was 51.5% (n=242), amounting to 4.0% of all cases where blood cultures were performed (Supplementary Figure 2). One study accounted for

151 of 242 cases of true positive blood cultures with changes in clinical management, including broadening antimicrobial therapy (51%), narrowing antimicrobial therapy (38.5%), increasing duration of antimicrobial therapy (51%), or recalling patients back to the hospital who had been previously discharged (8.4%) [11].

A single study in children with suspected appendicitis demonstrated a positive culture yield of 3.8% (11/288) [17]. However, 10 of the 11 cultures were determined to be contaminants by investigators, resulting in a single true case of bacteremia or a true positive yield of 0.34% from the total sample. No change in antimicrobial therapy or clinical management was documented for this patient. For adults, the certainty of evidence is very low due to: moderate risk of bias concerns (according to QUIPS assessment) [18] and serious concerns for indirectness due to a small proportion of patients suspected of an intra-abdominal infection among many other presentations to the emergency department (Supplementary Table 2). For children, the certainty of evidence is low due to risk of bias (according to QUIPS assessment) [18] and imprecision concerns. No studies assessing the impact of blood cultures on changes to antimicrobial management in pregnant patients were identified.

Three cohort studies examined in-hospital mortality among adult patients with a positive blood culture result [12,14,16]. Combined data for 1,337 adult patients demonstrated a positive culture yield of 31.3% (n=418), 23.9% of which were false positives (contaminants) based on investigator criteria. The Nakamura study [14] did not adhere to standard definitions for contaminants, [19] which likely contributed to the high false positive rate observed. This translated to a true positive yield of 23.8% (n=318) among the entire cohort. The weighted in-hospital mortality proportion was 15.9% (n=70) among patients with a true positive blood culture result and 3.8% among the entire cohort (Supplementary Figure 3). However, this varied widely between the three studies with 61 deaths reported in a single study [14]. Overall, patients with positive blood cultures (not contaminant) had a higher likelihood of in-hospital mortality compared to those with a negative or false positive blood cultures (OR 2.44, 95% CI: 1.70-3.49) (Supplementary Figure 4). The certainty of evidence is very low due to moderate risk of bias concerns (according to QUIPS assessment) [18], indirectness as mentioned above, and inconsistency due to wide variations in pre-test probability among the three studies. One of the included studies [16] was specific to patients with intra-abdominal infection (acute cholangitis). When analyzed separately, there were greater odds of in-hospital mortality (OR 7.89, 95% CI: 0.96-64.89) compared to the above pooled analysis of all studies, but this difference was not significant (p=0.28) (Supplementary Figure 5). An additional observational study reported a 30-day mortality rate of 11.5% (n=69) among adult patients with positive blood culture results collected in the emergency department [20].

No studies assessing in-hospital mortality in pediatric or pregnant patients with a positive blood culture were identified. In addition, none of the studies focused on patients with immunocompromising conditions.

Rationale for Recommendations

The decision to obtain a blood culture should primarily be based on clinical suspicion of sepsis and criteria that require hospitalization and monitoring. Sensitive, but poorly specific, signs of sepsis include hypotension, tachypnea, and delirium. Blood culture yield is optimized when drawn prior to antimicrobial therapy. Collection of blood cultures should not be delayed while trying to discern whether hypotension responds to fluids or whether delirium is new-onset. Prediction models, such as the Shapiro prediction rule, have been developed as supplemental tools for Emergency Department (ED) physicians to improve blood culture utilization [21]. However, these prediction models are not widely used and have not been robustly validated. Thus, the committee came to a consensus that using clinical signs and symptoms along with evidence from basic laboratory tests to determine who is at highest risk of sepsis can lead to more targeted utilization of resources than the use of prediction models [22]. In addition, the following scenarios may warrant the collection of blood cultures: high rates of regional resistance to commonly used agents administered as empiric treatment for intra-abdominal infections, patient history of any colonization or infection with organisms not susceptible to commonly used empiric regimens within the prior 90 days, or healthcare-asssociated infection.

When skin contaminants are excluded, the overall rate of blood culture positivity is lower for ED patients (3.8-13.3%) [11-13,23,21] compared to hospitalized patients (19.5%) [14]. When a primary source of infection is specified, intra-abdominal represents a small proportion of the patients with true bacteremia (<2-13%) [11,12,14,23] (Supplementary Table 3). Given the low yield of blood cultures for true positive results, there is a substantial risk of over-testing. While the analytical costs for blood cultures is relatively low, the clinical cost of positive results may be high for false-positive results, including inappropriate antibiotic use, increased downstream diagnostic testing, and longer hospital length of stay. Contamination of blood cultures during phlebotomy (including contamination by skin flora) is a relatively common occurrence, with a median contamination rate of 5.4% for the studies evaluated (range: 2.3-13.4%) [11,12-15,17,20,23] (Supplementary Table 3). The risk of false-positive cultures being acted on is mitigated by the use of rapid diagnostic tests, which have become standard of care. These tests provide a rapid identification of bacteria in blood cultures (i.e., <2 hours) and provide a means to rule out skin flora contaminants shortly after blood cultures flag positive. Furthermore, use of strategies to divert the first ~1 mL of blood drawn prior to culture, including blood culture collection devices, have been shown to decrease the number of false-positive cultures in many studies [24]. Thus, the recommendations were designed to balance the potential harms of contaminated (false-positive) blood culture results versus the potential benefits of detecting true positive bacteremia in patients under evaluation for intra-abdominal infection.

Implementation considerations

Prediction tools such as the Shapiro rule or Systemic Inflammatory Response Syndrome (SIRS) criteria are useful to reduce unnecessary blood cultures in immunocompetent patients but cannot replace clinical judgment [21,23,25]. Prediction tools specific to this population are not well validated in multicenter studies, and interfacility variability among emergency care settings may

lead to these tools being less predictive in certain settings. Outpatients being evaluated for intra-abdominal infections have a much lower risk of bacteremia than hospitalized or post-surgical patients. Patients (including children) with appendicitis rarely have bacteremia while those with cirrhosis and peritonitis, severe pancreatitis, or septic shock all have substantial risk [17]. In addition, for immunosuppressed patients, including the elderly or pregnant people, the potential clinical benefit of information gained from a positive culture may outweigh any potential risks of obtaining the blood culture. To ensure adequate sampling, at least two blood culture sets (each set consists of one aerobic and one anaerobic culture) from separate venipuncture draws should be collected from adults with suspected bacteremia [26,27]. For pediatric patients, weight-based blood collection guidelines should be followed; if only one bottle can be collected, it should be an aerobic culture [28]. To minimize blood culture contamination, specimen collection by a dedicated team of phlebotomists is recommended [29]. Rapid molecular technologies to identify common pathogens and resistance markers after a positive blood culture result have become standard in most facilities, enabling a rapid identification of contaminants [19,30].

Research needs

Further validation of clinical prediction rules for blood culture positivity of patients with suspected intra-abdominal infections is needed, as well as more studies on the utility of alternative biomarkers in prediction models (e.g., C-reactive protein, procalcitonin). The studies evaluated were published between 2005 and 2022, spanning past and current levels of antimicrobial resistance, which may have influenced results of the studies. The lack of rapid diagnostics that can identify pathogens responsible for particular syndromes (especially culture-negative cases) is an important gap. Further evaluation of the impact of cultures identifying multidrug-resistant organisms on the course of patient management and outcomes are needed. Finally, development of improved diagnostics for direct-from-specimen tests to detect organisms that cause bacteremia and their antimicrobial susceptibility are needed.

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recommendations and manuscript, and final approval of the recommendations and manuscript to be published. Jennifer Loveless, Katelyn Donnelly, and Sarah Pahlke, methodologists, were responsible for general project management, designing and performing the data analyses, and leading the panel according to the GRADE process.

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Additional information: More detailed information on the analysis and development of recommendations is available in the Supplementary Material.

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