

IDS A GUIDELINES

2024 Clinical Practice Guideline by the Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Utility of Intra-abdominal Fluid 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 cultures of intra-abdominal fluid 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; fluid culture; guideline

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

Recommendation: In adults and children with complicated intra-abdominal infection who are having a procedure for source control, the panel suggests obtaining intra-abdominal cultures to guide antimicrobial therapy (*conditional recommendation, moderate certainty of evidence*).

Remarks:

- When obtaining intra-abdominal cultures, fluid inoculation is the preferred method of collection.

Recommendation: In adults and children with uncomplicated appendicitis undergoing an appendectomy, the panel suggests not routinely obtaining intra-abdominal cultures (*conditional recommendation, low certainty of evidence*).

Remarks:

- Immunocompromised patients are at increased risk for antibiotic-resistant organisms and intra-abdominal cultures are generally warranted.
- At the time of surgery, if complicated disease is suspected/recognized, intra-abdominal cultures may be advised.

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 cultures of intra-abdominal fluid in adults and children. 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, which includes uncomplicated appendicitis, 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 culture of intra-abdominal fluid were considered; those with spontaneous bacterial peritonitis or cirrhosis were excluded. Studies evaluating change in antimicrobial therapy and prediction of mortality were included. Observational studies published after 2005 and randomized controlled trials were screened for inclusion. 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 literature search was conducted, and nine studies were identified addressing intra-abdominal fluid cultures and the outcomes of change in antimicrobial therapy and mortality for the targeted patient population.

Seven cohort studies examined how often peritoneal fluid culture results prompted a change in antimicrobial therapy in patients with appendicitis [11-17] (Supplementary Table 1). The yield of peritoneal fluid cultures varied across the studies, ranging from 11% to 92% of patients cultured, with most studies reporting a yield of ~40-50%. For uncomplicated appendicitis, one study reported no changes in antimicrobial therapy for 67 patients who received a fluid culture [13]. For complicated appendicitis, combined data for 171 patients (115 with positive fluid culture) demonstrated that culture results drove a change in antimicrobial therapy for 14 patients [13,15-17]. For studies that combined both uncomplicated and complicated appendicitis, 1 change in therapy was reported for 787 patients (289 with positive fluid culture) [11,12,14] (Supplementary Figure 2).

A multicenter study of 41,495 patients with complicated intra-abdominal infection found that obtaining a fluid culture was associated with increased escalation of antimicrobial agents on day 5 (adjusted OR 1.56, 95% CI: 1.42-1.72) [18] (Supplementary Figure 3). Importantly, in this study, obtaining a fluid culture was associated with improved survival (adjusted OR of mortality 0.85, 95% CI: 0.77-0.95) (Supplementary Figure 4). One study specifically evaluated the impact of *Candida* spp. isolation from peritoneal fluid cultures in patients with non-postoperative complicated intra-abdominal infection [19]. The prevalence of intra-abdominal candidiasis in the 442-patient cohort evaluated was 15.6%; of the 69 patients with intra-abdominal candidiasis, 52.2% were treated with an antifungal drug (constituting a change in antimicrobial therapy). In-hospital mortality was 21% in the group treated versus 33% in the untreated group ($p = 0.29$). When comparing those with and without *Candida*, *Candida* isolation was associated with higher all-cause mortality (OR 2.15, 1.03-4.46, $p = 0.04$) in multivariate analysis.

The certainty of evidence for the outcome of change in therapy is low due to risk of bias concerns (according to QUIPS assessment; Supplementary Table 2) [20,21] and indirectness, and the certainty of evidence for the outcome of mortality is high (Supplementary Table 3).

Rationale for Recommendations

For most patients with uncomplicated appendicitis, postoperative antibiotic therapy is not required, so obtaining a peritoneal fluid culture is unnecessary. Additionally, if a peritoneal fluid culture is obtained and incidentally positive (with no other signs/symptoms of infection), it may lead to unnecessary antimicrobial use.

For patients with complicated intra-abdominal infection, including complicated (perforated or gangrenous) appendicitis, positive peritoneal fluid cultures may provide useful information to guide antibiotic and/or antifungal selection. This is particularly true for patients who go on to fail therapy, experience a recurrence of infection, or are found to be infected with less common or multidrug-resistant microorganisms, including *Candida* spp. Additional benefits of targeted, narrow-spectrum therapy that is informed by culture data include the avoidance of drug-toxicity, *C. difficile* infections and exposure to broad-spectrum antibiotics that promote the emergence of antimicrobial resistance.

Implementation considerations

Though evidence specific to pregnant and immunocompromised patients was not identified, it would be reasonable to apply these recommendations to these populations.

If peritoneal cultures are collected, inoculation of the fluid into blood culture bottle(s) has consistently been shown to improve the likelihood of organism recovery [22-28]. Seven studies evaluating 1,351 patients compared peritoneal cultures performed by inoculation on solid growth media (e.g., blood agar, chocolate agar) to incubation in blood culture bottles. Patients evaluated included a predominance of those on continuous ambulatory peritoneal dialysis with peritonitis. Yield of cultures was 48% with the use of blood culture systems versus 37% by traditional methods (inoculating solid media only). Across these studies, recovery of Gram-negative bacteria, streptococci and enterococci were improved with the use of blood culture bottles. The amount of fluid inoculated should be in accordance with the manufacturer's instructions for use. If Gram-stain is desired and the sample is inoculated into a blood culture bottle, an additional specimen should be collected and submitted to the laboratory; alternatively, the fluid can be inoculated to the blood culture bottle by the laboratory. One study evaluated inoculation of bottles at bedside versus upon receipt of fluid in the laboratory and did not find a difference in yield [24]. In general, use of a swab to collect specimens results in suboptimal organism yields [25].

Research needs

While peritoneal cultures were found to rarely result in change in clinical management, the majority of studies only included patients with appendicitis. Additionally, the prevalence of multi-drug-resistant organisms within these studies was either very low or not reported. Future research should evaluate the value of peritoneal cultures in geographies/regions with higher antimicrobial resistance rates and in immunocompromised individuals.

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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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