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Update on blood cultures: how to obtain, process, report, and interpret

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Abstract

The detection and identification of microorganisms circulating in the bloodstream of patients is arguably one of the most important functions of the clinical microbiology laboratory. Effective implementation of this function requires careful consideration of specimen collection and processing, culture techniques, result reporting, and, perhaps most importantly, result interpretation by the physician. The purpose of this review is to provide a synopsis of the current state of the art for each of these areas, with the intention of providing adequate information to enable clinical laboratory personnel and physicians to critically evaluate and, if required, improve their current blood culture practices.

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Introduction

Bloodstream infections (BSIs) represent an important cause of human morbidity and mortality. The evaluation of patients suspected of having a BSI routinely includes blood cultures, which optimally yield an aetiological diagnosis and provide the opportunity to perform antimicrobial susceptibility testing to guide therapeutic intervention when necessary. The clinical significance of positive blood cultures has been extensively evaluated over the past several decades [1–6]. These studies have served to define the most frequent aetiological agents responsible for BSIs and the range of agents, and have improved our understanding of the risks and outcomes associated with such infections. As the baseline characteristics of patients have changed with advances in medicine (e.g. more immunocompromised hosts, more indwelling catheters and other intravascular devices, and changes in therapy for human immunodeficiency virus), the epidemiology of BSIs has also evolved, with more infections occurring in patients with intravascular devices and in outpatient settings [5]. Additionally, there appears to be a trend towards improved outcomes in patients with BSIs, perhaps as a consequence of earlier therapeutic intervention, whereas the number of BSIs appears to be increasing, especially those occurring in populations that were previously less affected (outpatients).

Because BSIs remain an important cause of morbidity and mortality, and prompt targeted therapeutic intervention may improve patient outcomes, there has been significant interest in improving the speed and accuracy of blood culture methods in the clinical microbiology laboratory. Despite these efforts, little has changed since the introduction of continuous-monitoring blood culture systems in the 1990s, but incremental advances in more rapid identification and susceptibility prediction have occurred, especially for some particularly troublesome pathogens. Moreover, greater advances appear to be on the horizon.

Blood Culture Collection

The utility of blood culture for detecting BSI is directly influenced by the collection of optimal specimens only from patients with clinical findings compatible with BSI; routine 'surveillance' blood cultures are costly and of little clinical value [7–9]. Clearly, venipuncture is the preferred method for blood

culture collection. Arterial blood samples do not increase diagnostic yield, and blood specimens obtained from intravascular lines have demonstrated increased rates of contamination in some studies [10]. The American College of Physicians guidelines recommend that collecting blood for culture from intravascular devices be avoided, and the CLSI recommends that, if one must collect a blood culture from an intravenous line, it should be paired with a culture that is obtained via venipuncture to assist in the interpretation of positive results [11,12]. The timing of blood culture collection does not appear to significantly affect the recovery of clinically relevant microorganisms, and most authorities therefore recommend collecting multiple sets simultaneously or over a short period of time, except when documentation of continuous bacteraemia is required for patients with endovascular infection [12,13]. Whenever possible, two to four sets of blood specimens should be collected from independent venipuncture sites, and, for adult patients, each set should consist of 20–40 mL of blood [12–15]. The volume of blood drawn from infants and children is less well prescribed, but should be based on the child's age and not exceed 1% of the patient's total blood volume [12,16]. It is clear that the total volume of blood cultured from adult patients is directly proportional to the yield of microorganisms recovered. This is a consequence of the fact that most adult patients with BSIs have very low circulating concentrations of viable microorganisms. Inadequate blood volume or the collection of a single blood culture set significantly reduces the sensitivity of the test, and also makes the interpretation of results far more difficult [13,15,17,18]. Collection of multiple sets of blood cultures from a single venipuncture or intravascular line should also be avoided. For optimal recovery of diverse BSI aetiological agents, each set of blood cultures should include paired aerobic and anaerobic blood culture bottles, and the aerobic bottle should be filled first [12,19,20].

Proper skin antisepsis prior to collection of blood cultures via peripheral venipuncture is paramount, to reduce blood culture contamination rates and facilitate result interpretation for the clinician. A variety of skin disinfectants have been clinically evaluated, and reports comparing their relative efficacy have been published [21–25]. On the basis of these data, current guidance documents conclude that tincture of iodine, chlorine peroxide and chlorhexidine gluconate are superior to povidine-iodine preparations, and that tincture of iodine and chlorhexidine gluconate are probably equivalent for skin antisepsis prior to blood culture collection [12]. Although chlorhexidine gluconate is an adequate disinfectant for older infants, children, and adults, it should not be used on infants <2 months of age, and an alternative is therefore required in centres where this disinfectant is otherwise routinely employed.

Once optimal blood culture specimens are collected according to the principles outlined above, they should be sent to the laboratory as promptly as possible. These specimens should never be refrigerated or frozen, and should be held at room temperature for no more than a few hours if necessary. Although an extended delay between blood culture collection and incubation in a continuous-monitoring blood culture instrument is not recommended, a significant diminution in pathogen recovery has only been experimentally observed when blood culture bottles have been held for >24 h at 4°C or room temperature and for >12 h at 37°C [26]. Lengthy incubation of blood culture bottles prior to entering them into a continuous-monitoring blood culture instrument may delay or impede the detection of growth by the instrument, and is discouraged.

Laboratory Techniques for Blood Culture

In the vast majority of institutions, most blood culture specimens delivered to the laboratory are entered into an incubation protocol on a continuously monitored blood culture device. There are several manufacturers of such devices, and their performance characteristics are similar [27–35]. These devices incubate the blood culture bottles for a prescribed period of time (determined by the user) and signal audibly and/or visually if growth is detected.

Each automated blood culture system has its own associated medium formulations that must be selected by the user. The blood culture bottles typically contain proprietary mixtures of culture medium, an anticoagulant, and, in many cases, resins or charcoal mixtures to reduce the effects of antimicrobials and other toxic compounds. Generally, combinations of medium formulations that are complementary to each other are chosen to enhance the recovery of the most diverse range of microorganisms. Medium combinations typically include aerobic and anaerobic formulations and, in select circumstances, a formulation containing reagents that are ideal for recovering mycobacteria and/or yeasts may be inoculated as well. Controlled studies comparing the performance of media with and without the addition of antimicrobial binding or absorbing agents (resins and/or charcoal compounds) have repeatedly demonstrated that the latter formulations are clearly superior for the recovery of microorganisms, especially staphylococci and yeasts [29,34–37].

Blood cultures entered into automated, continuous-monitoring protocols should routinely be incubated for 5 days. Multiple studies have shown that this incubation time is adequate for the detection of the majority of pathogens, including fastidious bacteria that belong to the *Haemophilus*,