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Guideline

# Guidelines on Blood Cultures

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Just over one-third of sepsis patients have positive blood cultures, mainly due to inadequate sampling volumes (50% of adults have < 1.0 CFU/mL blood) and the prior use of antibiotics. However, 20–30% of sepsis patients are given inappropriate empirical antibiotics. The Clinical and Laboratory Standards Institute guidelines recommend paired culture sets to help discriminate between contaminant organisms and true pathogens; four 10-mL bottles (2 sets) should be used for the initial evaluation to detect about 90–95% of bacteremias and six 10-mL bottles (3 sets) should be used to detect about 95–99% of bacteremias. It has also been shown that the positivity rate increased by 15–35% with resin-based media in patients on antibiotics. For diagnosing catheter-related bloodstream infections, differential time-to-positivity is one method recommended to help determine whether the catheter is truly the source of infection. The proper training of personnel with regard to drawing an appropriate blood volume and the importance of clear labeling of culture bottles is also of critical importance. Furthermore, if the contamination rate is relatively high, hiring dedicated staff who are well-trained in order to get a lower blood culture contamination rate may be cost-effective. It is because high false-positive blood culture rates due to contamination are associated with significantly increased hospital and laboratory charges.

**KEYWORDS:** antibiotics, bacteremia, blood cultures, resin-based media

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## Introduction

Patients with sepsis, defined as a clinical infection resulting in a systemic inflammatory response, are not always culture-positive, with only about one-third overall having positive blood cultures. This can be due to local containment of the infection, poor timing of collection, insufficient blood volumes being cultured, or because patients are given antibiotics prior to blood cultures being obtained.[1,2] Nevertheless, there is a general consensus in Taiwan and internationally that it is important to optimize organism

recovery to facilitate the management of suspected sepsis patients, of whom an estimated 20–30% are given inappropriate initial empirical antibiotics.

Adequate sampling volume is the single most important factor for detecting a bloodstream organism, particularly in adults, since 50% of patients have < 1.0 CFU/mL of blood. The Clinical and Laboratory Standards Institute (CLSI) guidelines recommend four 10-mL bottles of blood be taken for the initial evaluation in order to detect about 90–95% of patients with documented bacteremia; and a 95–99% detection rate would require 60 mL of blood to be cultured.[3,4]

Another critical factor preventing identification of bacteremia is that patients are frequently already on antibiotics when the first sample is drawn, giving negative cultures. Combined with inadequate sampling volumes, this can lead to a vicious cycle of misdiagnosis and inappropriate treatment.[5]

Therefore, it is important to obtain blood cultures prior to starting empiric antibiotic therapy to optimize the chances of pathogen recovery. If the patient has already been administered antibiotics, however, it makes it critical to use a system of culture media that effectively neutralizes antibiotics, increasing the chance of pathogen recovery.

The BACTEC Aerobic/Anaerobic Plus resin media system (Becton, Dickinson and Company, Sparks, MD, USA) contains two different types of resin which bind and neutralize a wide variety of antibiotics. In patients already on antibiotics, there is a significantly increased positivity rate, ranging from 15% to 35%, when resin-based media are used to neutralize antibiotics and allow pathogen recovery, compared with non resin-based culture media.

CLSI guidelines also recommend that a single set of cultures should never be drawn initially in patients with clinical suspicion of sepsis, particularly from a catheter, not only because there will be inadequate volume, but also because additional, independently-drawn venipuncture sets help to discriminate between contaminant organisms such as *Staphylococcus epidermidis* and true pathogens.

## Discussion

The diagnosis and treatment of patients with subacute bacterial (infectious) endocarditis (SBE) can be particularly problematic. However, it is important to try to establish the microbiological diagnosis and its susceptibility profile before starting long-term, intravenous antimicrobial therapy. Because SBE is a subacute infection, three blood culture sets are performed initially, since there is no need to start empiric antibiotic therapy immediately. After having performed three culture sets, it is appropriate to observe the patient, who will have been admitted to hospital. If blood culture sets are negative the following day, taking another two or three culture sets increases the chances of recovering the organism and making a microbiological diagnosis; although blood cultures may still be negative, even after the fifth or sixth culture. Importantly, the leading cause of culture-negative SBE is current antimicrobial administration; thus, the use of resin-based media is advisable to effectively neutralize antibiotics and allow recovery of pathogens.

There are some differences in the efficacy of resin-based culture media regarding their ability to neutralize different antibiotic agents available, including antibacterials and antifungals. Although the resins have a relatively broad spectrum of activity, they may occasionally not neutralize some antibiotics as well as others.

In the majority of hospitals in Taiwan, two or three initial blood culture sets are ordered, as recommended by the CLSI blood culture guidelines. This is a standard practice because the National Health Insurance scheme in Taiwan reimburses a proportion of all hospital charges, including laboratory fees. However, while this is true for hospitals, not all physicians in Taiwan will necessarily order two initial blood culture sets.

To confirm a suspected diagnosis of a catheter-related infection, several issues should be considered. In both the CLSI blood culture guidelines and the Infectious Disease Society of America recommendations for diagnosing catheter-related bloodstream infections, differential time-to-positivity is one of the methods recommended to help determine whether the catheter is truly infected. This is important, since in the United States, up to 70% of central lines are removed unnecessarily because they are wrongly thought to be infected. The basic premise is that, if the catheter is the site of the infection, there will be more CFU per mL bacteria in blood drawn from the catheter, and it will show positive 2–3 hours prior to peripherally-drawn cultures, suggesting that the catheter is the source of the bloodstream infection.

The proper training of personnel with regard to drawing an appropriate blood volume and the importance of clear labeling of culture bottles is also of critical importance. Furthermore, if the contamination rate is relatively high (with false-positives over 3%), it may be cost effective to hire dedicated staff who are well-trained in order to get a lower blood culture contamination rate. It is because high false-positive blood culture rates due to contamination are known to be associated with a significant increase in hospital and laboratory charges.[6]

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