Blood Cultures for the Detection of Bacteremia

Abstract: A blood culture is a test that checks for foreign invaders like bacteria, yeast, and other microorganisms in one's blood. Having these pathogens in one's bloodstream can be a sign of a blood infection, a condition known as bacteremia. A positive blood culture means that you have bacteria in one's blood. In this article, issues related to types of bacteremia, indications, and technique for blood cultures will be reviewed here.

Keywords: blood culture, bacteria, yeast.

INTRODUCTION

Blood is one of the most important specimens received by the microbiology laboratory for culture, and culture of blood is the most sensitive method for detection of bacteremia or fungemia. Issues related to types of bacteremia, indications, and technique for blood cultures will be discussed.

INDICATIONS FOR CULTURES

Blood cultures are ordered when one's doctor suspects you may have a blood infection. It's important to test for blood infections because they can lead to serious complications. One such complication of a blood infection is sepsis. Blood cultures should be obtained prior to initiation of antimicrobial therapy for any patient in whom there is suspicion of bacteremia, including hospitalized patients and selected outpatients with fever and leukocytosis or leukopenia (Coburn, B. et al., 2012). However, a normal white blood count does not rule out bacteremia (Seigel, T. A. et al., 2012; & Fu, C. M. et al., 2012). Circumstances in which blood cultures are especially important include sepsis, meningitis, osteomyelitis, arthritis, endocarditis, pneumonia, and fever of unknown origin.

METHOD FOR OBTAINING CULTURES

In general, patients with bacteremia are likely to have low quantities of bacteria in the blood, even in the setting of severe clinical symptoms. For this reason, multiple blood cultures, each containing large volumes of blood, are required to detect bacteremia. Prior to initiation of antimicrobial therapy, separate venipuncture sites should be obtained (Weinstein, M. P. 1996). The technique, number of cultures, and volume of blood are more important factors for detection of bacteremia than timing of culture collection.

Technique

Careful technique is important to avoid contamination of the blood culture media by normal skin flora during the process of collection. This is important because normal bacterial skin flora can cause systemic disease such as infective endocarditis, and in some circumstances blood culture contamination can make it difficult to distinguish between false positive results and true infection. Important measures to reduce contamination include effective disinfection of the venipuncture site and avoiding blood culture collection through existing intravenous lines (Little, J. R. et al., 1999; Strand, C. L. et al., 1993; Mimoz, O. et al., 199; Schifman, R. B., & Pindur, A. 1993; & Tafuro, P. et al., 1986).

The tourniquet should be applied and the vein palpated before disinfection of the venipuncture site. Thereafter the venipuncture site should be cleansed with 70 percent alcohol followed by 1 to 2 percent tincture of iodine or chlorhexidine (Little, J. R. et al., 1999; Strand, C. L. et al., 1993; Mimoz, O. et al., 1999; Schifman, R. B., & Pindur, A. 1993). The disinfectant should be allowed to dry for one to two minutes before blood is aspirated. If further palpation of the vein is necessary after skin preparation, a sterile glove should be worn (Archibald, L. K. et al., 2006). Alcohol should be used to disinfect the septum of culture bottles after removal of their flip caps. Blood should be collected directly into culture bottles during the venipuncture procedure, rather than into transport tubes sent to the laboratory for subsequent transfer of blood into the culture bottles.
Lower contamination rates have been observed with iodine tincture and chlorhexidine than with povidone-iodine (Little, J. R. et al., 1999; Strand, C. L. et al., 1993; Mimoz, O. et al., 1999). A randomized trial comparing iodine tincture with povidone-iodine in over 3800 blood cultures obtained from adult inpatients reported a lower contamination rate with iodine tincture (2.4 versus 3.8 percent) (Little, J. R. et al., 1999). A randomized trial comparing chlorhexidine with povidone-iodine in over 2000 blood cultures reported a lower contamination rate with chlorhexidine (1.4 versus 3.4 percent) (Mimoz, O. et al., 1999).

Blood cultures should not be drawn through an intravenous catheter at the time of catheter insertion. In an observational study of over 4100 blood cultures obtained for evaluation of children with suspected bacteremia, the false positive rate was higher for specimens obtained at the time of catheter insertion than for specimens obtained from a separate site (9.1 versus 2.8 percent) (Norberg, A. et al., 2003).

Drawing blood for cultures through an indwelling intravascular catheter should be avoided whenever possible, since ports are frequently colonized with skin flora, thereby increasing the likelihood of a false positive blood culture. If blood cultures are drawn from an intravenous line, a second specimen should be drawn from a peripheral venipuncture. Arterial blood cultures provide the same yield as venous blood cultures.

Number of cultures

The optimal number of blood cultures that should be obtained at initial evaluation varies with the clinical condition, suspicion of underlying infection (eg, the pretest probability), and the urgency of the need for treatment (Lee, A. et al., 2007). In addition, the number of cultures obtained depends on the volume of blood drawn for each culture set. Among 134 patients in one study, the yield from two blood cultures (30 mL in each of two bottles) was the same as the yield from three blood cultures (20 mL in each of three bottles) (Patel, R. et al., 2011). In two other studies evaluating yield for four or more blood cultures (volume 20 mL), the cumulative yield of true pathogens increased with the first (73 to 80 percent), second (80 to 89 percent), third (95 to 98 percent), and fourth (99 to 100 percent) cultures collected (Lee, A. et al., 2014; & Cockerill III, F. R. et al., 2014).

One blood culture set is rarely advisable or sufficient. A positive single culture result may be uninterpretable unless an unequivocal pathogen is isolated. If a possible contaminant is reported on a single culture, additional culture data are needed, and in the interim, unnecessary antimicrobial therapy or unnecessary testing may not be pursued. Moreover, a single blood culture lacks sensitivity as well as precludes the ability to distinguish contaminants from true bacteremia with bacteria that are common contaminants (ie, specificity), eg, coagulase-negative staphylococci and diphtheroids (Mirrett, S. et al., 2001). A total of two blood culture sets is usually adequate when bacteremia due to a pathogen not likely to be a contaminant is anticipated (as in intraabdominal sepsis or pneumonia) and when the pretest probability of bacteremia is low to moderate. Samples should be obtained by at least two separate venipunctures. A total of three blood culture sets is usually adequate when a continuous bacteremia is suspected and the pretest probability of bacteremia is high (as in patients with suspected infective endocarditis who have not received prior antimicrobial therapy).

Four blood culture sets is reasonable when the pretest probability of bacteremia is high and the anticipated pathogen is likely to be a common contaminant, such coagulase-negative staphylococci. Clinical examples include prosthetic valve endocarditis or endovascular infections due to infected devices, such as pacemakers or grafts. Four blood culture sets may also be necessary to diagnose endocarditis in patients who have received antimicrobial therapy in the preceding two weeks. Additional blood cultures are rarely useful in patients who have been evaluated by the above criteria unless there has been a significant change in the patient's condition or a new focus of infection is suspected. Furthermore, the chance of obtaining a false-positive test (ie, a positive blood culture due to a contaminant) increases steadily as more blood cultures are obtained.

Volume of blood

The blood culture yield depends on the volume of blood cultured (Connell, T. G. et al., 2007; Ilstrup, D. M., & Washington II, J. A. 1983; & Mermel, L. A., & Maki, D. G. 1993). One study comparing 829 matched pairs of standard volume (mean 8.7 mL) and low volume (mean 2.7 mL) blood cultures demonstrated that bottles inoculated with at least 5 mL of blood had a significantly higher detection rate for blood infection than bottles inoculated with less than 5 mL (92 versus 69 percent) (Mermel, L. A., & Maki, D. G. 1993). The authors estimated that the yield of blood cultures in adults increases approximately 3 percent per mL of blood cultured. The appropriate volume for adults is a minimum of 10 mL (and preferably 20 mL) of blood.

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Recommended blood volume

<table>
<thead>
<tr>
<th>Weight of patient (kg)</th>
<th>Recommended volume of blood for culture (mL)</th>
<th>Blood culture bottle used</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 - 2</td>
<td>1 - 2</td>
<td>Paediatric (yellow top)</td>
</tr>
<tr>
<td>2.1 – 13</td>
<td>4</td>
<td>Paediatric (yellow top)</td>
</tr>
<tr>
<td>13 – 36</td>
<td>8 - 10</td>
<td>Adult (green top) or x 2 Paediatric (yellow top)</td>
</tr>
<tr>
<td>&gt;36.1</td>
<td>20</td>
<td>Adult (green top) x 2</td>
</tr>
</tbody>
</table>

Max volume into specimen bottle: BactT/Alert Paediatric 4ml, BacT/Alert Standard Aerobic (adult) 10ml

Paediatrics and neonates blood culture bottle

Adult blood culture bottles

Timing

Fever at the time of blood culture collection is neither sensitive nor specific for the presence of bacteremia. In a retrospective study evaluating the timing of blood culture collection in relation to temperature elevations in over 1400 patients with bacteremia and fungemia, no relationship was observed between timing of specimen collection and likelihood of a positive blood culture (Riedel, S. et al., 2008). There is no difference in yield whether blood samples for culture are drawn simultaneously or at intervals spaced within a 24 hour period. For patients who are acutely ill or have high likelihood of continuous bacteremia, it is appropriate to obtain blood cultures from two separate sites within minutes of one another (Weinstein, M. P. 1996). Blood cultures should be obtained prior to initiation of antibiotic therapy.

CULTURE MEDIA

Special culture media may be helpful in the following settings:

- Cultures containing resins, lytic agents, or other neutralizing substances may be useful for detecting yeast.
- Dimorphic fungi, especially Histoplasma capsulatum, are best detected from blood with the centrifugation-lysis (Isolator) system, which is also useful in the detection of Mycobacterium avium and Mycobacterium tuberculosis.
- Special broth media (BACTEC) are also available for the detection of mycobacteria species.

INTERPRETING POSITIVE CULTURES

Types of bacteremia

There are two clinical patterns of bacteremia, intermittent and continuous:

- Intermittent bacteremia implies that bacteria are present in the blood for periods of time followed by nonbacteremic periods; this is the most common pattern of bacteremia. It can occur following manipulation of infected tissues (such as surgical abscess drainage), following instrumentation of contaminated mucosal surfaces (such as dental procedures, cystoscopy, or sigmoidoscopy), or in the setting of bacterial infections such as pneumonia, arthritis, osteomyelitis and meningitis.
- Continuous bacteremia usually reflects a persistent endovascular infection such as endocarditis or endarteritis, suppurative thrombophlebitis, or an infected aneurysm. It also occurs in the first two
weeks of typhoid fever and brucellosis though in these diseases relatively few bacteria per mL of blood are detected.

- There are two major categories of infection associated with bacteremia: extravascular infection and intravascular infection. Extravascular infections originate outside the bloodstream (such as pneumonia or urinary tract infection) and enter the vascular supply via the lymphatic system. Intravascular infections are associated with a primary infectious process within the bloodstream; examples include infective endocarditis, suppurative thrombophlebitis, and endovascular catheter infections. The efficiency of bacterial clearance depends on the infecting microorganism and the host immune status. For example, bacterial capsules and other virulence factors may delay clearance by decreasing opsonization, while the presence of specific antibodies may enhance clearance by promoting opsonization.

**Contamination**

Contamination of blood cultures can occur even when precise techniques for collection and processing are used. Contamination rates of less than 3 percent are desired; higher rates should be investigated and corrected with educational efforts (Richter, S. S. et al., 2002). Staphylococcus aureus, Streptococcus pneumoniae, group A streptococci, Enterobacteriaceae, Haemophilus influenzae, Pseudomonas aeruginosa, Bacteroidaceae, and Candida species are always important clinical pathogens (Pien, B. C. et al., 2010). Viridans streptococci and enterococci may reflect true pathogens or contaminants. Organisms for which it can be difficult to distinguish between pathogenicity and contamination include Propionibacterium acnes, Corynebacterium species, Bacillus species, and coagulase-negative staphylococci; the likelihood of pathogenicity is increased if the organism is observed in multiple blood cultures obtained by independent venipunctures. Blood cultures should be obtained PRIOR to initiation of antimicrobial therapy for any patient in whom there is suspicion of bacteremia, including hospitalized patients and selected outpatients with fever and leukocytosis or leukopenia. However, a normal white blood count does not rule out bacteremia. Circumstances in which blood cultures are especially important include sepsis, meningitis, osteomyelitis, arthritis, endocarditis, pneumonia, and fever of unknown origin. Prior to initiation of antimicrobial therapy, at least two sets of blood cultures taken from separate venipuncture sites should be obtained. The technique, number of cultures, and volume of blood are more important factors for detection of bacteremia than timing of culture collection. Important measures to reduce contamination include effective disinfection of the venipuncture site and avoiding blood culture collection through existing intravenous lines. There are two clinical patterns of bacteremia, intermittent and continuous. Intermittent bacteremia implies that bacteria are present in the blood for periods of time followed by nonbacteremic periods; this is the most common pattern. Continuous bacteremia usually reflects a persistent endovascular infection such as endocarditis. Organisms for which it can be difficult to distinguish between pathogenicity and contamination include Propionibacterium acnes, Corynebacterium species, Bacillus species, and coagulase-negative staphylococci; the likelihood of pathogenicity is increased if the organism is observed in multiple blood cultures obtained by independent venipunctures.

**REFERENCES**


