EDUCATIONAL COMMENTARY – UPDATE ON BLOOD CULTURES

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Learning Outcomes
Upon completion of this exercise, the participant should be able to:

- list and discuss seven indicators used to determine whether an organism isolated from a blood culture is a contaminant or a pathogen.
- discuss strategies to prevent contamination of blood cultures.

Since the 1980’s, three developments have impacted the detection of organisms in blood samples, and the interpretation of positive blood cultures. First, the number of patients with compromised immune systems due to infection with HIV, chemotherapy for malignancy, or therapy to suppress the immune response after organ transplant has increased substantially. Second, is the increased use of indwelling catheters in patients. Third, there have been considerable improvements made with blood culture media and instrumentation. The growing number of patients with compromised immune systems and the more frequent use of indwelling catheters, increases the likelihood of a patient acquiring an infection of the blood, and simultaneously more difficult to distinguish a true infection from contamination. Improvements in media and instrumentation have shortened the incubation time for a positive result, but they may have also impacted the volume of blood and the number of cultures needed for optimal results.

Detection of Contamination
Hall and Lyman\(^3\) reviewed the research on blood culture contamination and identified seven clues to help distinguish contamination from a true bloodstream infection:

1. Identity of the organism
2. Number of positive culture sets
3. Number of positive bottles within a culture set
4. Time to growth
5. Quantity of growth
6. Clinical and laboratory data
7. Site of culture

Of these seven indicators, the identity of the organism is most important for distinguishing contamination from infection because certain organisms correlate highly with infection or contamination (Table). However, the identity of the organism is not definitive and determining whether an organism that is usually a contaminant is the cause of a bloodstream infection can be challenging. For example, coagulase-negative staphylococci are both the most common blood culture contaminants and one of the most frequent causes of bacteremia. By contrast, of the organisms listed
in the Table as usual contaminants: *Corynebacterium* sp., *Propionibacterium acnes*, and *Bacillus* sp., other than *Bacillus anthracis*, are almost never implicated in infections. Finally, although blood cultures that contain more than one organism are often judged to be contaminated, this is not always the case. Hall and Lyman\(^3\) cite studies that conclude that as many as one in five cases of bacteremia involve multiple organisms, especially in patients at high risk.

In addition to the identity of the organism, the number of positive blood culture sets provides a further clue as to whether an organism is a likely contaminant, or a likely pathogen. Studies have consistently shown that the probability that an organism is a true pathogen correlates directly with the number of cultures in which it grows: the greater the number of cultures that yield the same organism, the greater the likelihood that it is a pathogen. For many years, two or three blood cultures obtained within a 24-hour period were considered adequate to detect bloodstream infections, because studies have shown that three blood cultures detect >99% of bloodstream infections. However, the results of recent studies suggest that the practice of collecting only two or three cultures may no longer be valid. Lee and colleagues\(^4\) in 2007 published results of a study in which they conclude that as many as four blood cultures may be needed to detect >99% of bloodstream infections. This supports the conclusion of Cockerill and colleagues\(^1\), who found that two or three blood cultures detected only 80% to 96% of cases of bacteremia. Cockerill and colleagues\(^1\) offer two possible explanations for this unexpected finding. First, because newer systems detect lower levels of bacteremia, a greater volume of blood (i.e., more cultures) may now be needed to detect sporadic low-level bacteremias. Alternatively, because more patients are now on antimicrobial therapy when blood cultures are obtained, more blood cultures may be needed because the antibiotics interfere with microbial growth. Although Lee and colleagues\(^4\) support the conclusions of Cockerill and colleagues\(^1\), they suggest that methodologic artifact due to differences in methods between the recent and earlier studies could account for the unexpected finding that more cultures are needed.

Another indicator used by many laboratorians and clinicians to identify contamination is the number of positive bottles in a blood culture set. Generally, more positive bottles are thought to correlate with a higher likelihood that the organism is a pathogen. However, as Hall and Lyman\(^3\) point out, since a blood culture set usually consists of one aerobic bottle and one anaerobic bottle, it seems reasonable that a particular organism would be more likely to grow in the bottle that best provides its needed growth conditions. Consequently, growth only in a single bottle does not necessarily mean that the organism is a contaminant. Research examining the correlation between the number of positive bottles and the likelihood of true bacteremia has yielded mixed results. For example, one study found that the number of positive bottles did predict the likelihood of true infection, and yet, another study found no significant correlation. However, studies have found that aerobic bottles consistently perform better than anaerobic bottles for both recovery and detection time for overall organisms.

Research on the reliability of using time to growth and quantity of growth to differentiate contamination from infection has also yielded mixed results. Blood samples obtained from patients with bacteremia...
are believed to have larger inoculums of bacteria than contaminated samples. As a result of the higher inoculums, cultures drawn from patients with sepsis theoretically should grow faster and yield greater quantities than contaminated cultures. Although several studies appear to support this theory, others fail to find time to growth to be a useful parameter to detect contamination. Researchers have also pointed out that low colony counts are often significant, especially in high-risk patients. Also, as technology continues to improve, the threshold sensitivity and time to detection are likely to decrease further. Thus, time to growth and quantity of growth are likely to become even less-reliable indicators of infection versus contamination.

Physicians often use clinical information to help interpret blood culture results. Signs of sepsis include fever, hypothermia, decreased or increased white blood cell counts, rigors, and hypotension. Other variables include coexisting diseases or a history of intravenous drug abuse. In the 1990s, the authors of several studies concluded that C-reactive protein measurements can serve as a surrogate marker for bloodstream infection. Today, as many as 30% of physicians in neonatal intensive care units routinely order this test to help predict sepsis.

Studies examining whether blood cultures drawn from indwelling catheters are more likely to be contaminated than those drawn directly from a vein have also yielded conflicting results. Some studies appear to show that cultures obtained from catheters are more often contaminated than cultures obtained directly from veins. Other studies fail to show significantly increased rates of contamination in cultures drawn from catheters. This issue is further complicated by the fact that a substantial number of indwelling catheters may be colonized by bacteria, which makes the interpretation of positive results more difficult. To help judge the significance of organisms isolated from blood cultures obtained from indwelling catheters, many physicians order at least one set obtained percutaneously.

In addition to these seven conventional clues, some investigators believe information technology shows promise as a tool to help interpret blood culture results, aid clinical decision making, and track contamination rates both within and between institutions. Although research in this area has been encouraging, more studies are needed to learn how to best implement this aspect of technology into clinical practice.

**Prevention of Contamination**

The most effective strategy an institution can adopt to prevent blood culture contamination is to ensure that all persons who collect blood cultures are properly trained. Studies have shown that trained personnel contaminate substantially fewer specimens than untrained personnel. The blood collection procedure should include explicit instructions that clarify how to disinfect the skin and blood culture bottles, whether to use a single- or double-needle technique, which site to choose for the blood draw, how much blood to collect, and which materials should be used to prepare the skin and collect the specimen. Trainers should ensure that phlebotomists understand the instructions and emphasize that all steps in the procedure must be rigorously followed.
The first step in obtaining a blood culture—disinfecting the skin—is most important. Inadequate skin preparation is the most common cause of contaminated blood cultures. Four common skin antiseptics are povidone-iodine, tincture of iodine, isopropyl alcohol, and povidone-iodine plus ethyl alcohol. These vary in the length of time the antiseptic must be in contact with the skin for maximum effectiveness, so it is critical that phlebotomists adhere to the recommended time for the antiseptic they are using. Skin that is obviously dirty should be cleansed thoroughly before applying the antiseptic. This will ensure that the antiseptic has good contact with the skin, thus maximizing its effectiveness.

In addition to disinfecting the skin, the caps of the blood culture bottles should be disinfected before the blood specimen is inoculated. Iodine alone should not be used for this purpose, because it may damage the rubber stopper. Instead, alcohol or an iodine solution, followed by alcohol, are often used.

Blood cultures were traditionally collected using a double-needle technique. In this method, the needle used to collect the sample is discarded and a new needle is used to inoculate the bottle. This method was largely abandoned with the emergence of the HIV virus in the late 1980’s because of the risk of needle stick injury. However, studies have shown that the double-needle technique is superior to the single-needle technique in reducing contamination. Improved needle design and vacuum-activated transfer devices have also decreased the risk of needle stick injury. As to whether this will result in greater use of the double-needle technique again, is uncertain.

Blood cultures are often collected from indwelling catheters, but this is a controversial practice for two reasons. First, catheters may be more difficult to disinfect, which may increase the likelihood of contamination. Second, catheters may be colonized, which can make a positive result more difficult to interpret. For these reasons, Hall and Lyman recommend obtaining blood cultures directly from a vein whenever possible. However, venous access is often difficult, especially in neonates, and an indwelling catheter is sometimes the only way to obtain an adequate specimen. Also, use of an indwelling catheter eliminates the pain of an additional venipuncture and reduces the chance of causing a transient bacteremia by the venipuncture. A study by Gonsalves and colleagues published in 2009 appears to support the practice of obtaining blood cultures from indwelling catheters. The researchers found no significant difference in contamination rates regardless of whether the specimen was obtained from venipuncture, arterial puncture, or central venous catheter. They did find, however, that specimens with inadequate blood volume were more likely to be contaminated.

Finally, the use of commercial blood collection kits may reduce the risk of contamination, although not all studies support this conclusion.

Summary

Blood cultures are an important tool to detect bloodstream infections, but interpretation of positive results can be difficult. Common contaminants can cause bacteremia in susceptible patients and
colonization of catheters can complicate the interpretation of positive results. Improved technology and media can detect lower numbers of bacteria, but this makes interpretation of a positive result more difficult and may paradoxically increase the number of cultures required for optimal results. Of the seven clues identified by Hall and Lyman\(^3\), the identification of the organism and the number of positive blood culture sets correlate the most with infection or contamination. Studies of the number of positive bottles in a set, time to growth, quantity of growth, use of clinical and laboratory data, and the site from which the culture was obtained have yielded conflicting results. Laboratories should consider these factors when developing blood culture protocols for their institutions.

TABLE. Correlation of Organism Identity With Infection or Contamination.

<table>
<thead>
<tr>
<th>Always a pathogen</th>
<th>Usually a pathogen</th>
<th>Usually a contaminant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>Streptococcus pyogenes</td>
<td>Coagulase-negative staphylococci</td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>Streptococcus agalactiae</td>
<td>Corynebacterium sp</td>
</tr>
<tr>
<td>All Enterobacteriaceae</td>
<td>Listeria monocytogenes</td>
<td>Bacillus sp other than Bacillus anthracis</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Neisseria meningitidis</td>
<td>Propionibacterium acnes</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>Neisseria gonorrhoeae</td>
<td>Micrococcus sp</td>
</tr>
<tr>
<td>Haemophilus influenza</td>
<td>Bacteroides fragilis group</td>
<td>Viridans group streptococci</td>
</tr>
<tr>
<td>All Candida sp</td>
<td>All Candida sp</td>
<td>Enterococci</td>
</tr>
<tr>
<td>Cryptococcus neoformans</td>
<td>Cryptococcus neoformans</td>
<td>Clostridium perfringens</td>
</tr>
</tbody>
</table>

References and Suggested Reading


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