# Antimicrobial Stewardship News

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## To Treat or Not to Treat? How to Identify Contaminated Blood Cultures

### Introduction

Blood cultures are required for diagnosing bloodstream infections (BSI) in patients with evidence of systemic disease. However, several factors must be considered in the clinical interpretation of blood culture results: type of pathogen, number of blood cultures collected, whether or not each set was collected from a separate site and labeled appropriately, and adherence to sterile technique. Contaminated blood cultures are associated with serious negative outcomes for patients, including increased costs and lengths of stay as well as unnecessary empiric antibiotic exposure while awaiting culture speciation and antimicrobial susceptibilities.[1-4] Despite the availability of guidelines outlining proper specimen collection, handling, and processing techniques as measures to prevent contamination, there is no official guidance to differentiate true pathogens from contaminants.[5-8]

This newsletter will describe the process for working up patients with positive blood cultures and differentiating true pathogens from possible contaminants.

### Blood Culture Basics

The Clinical Laboratory Standards Institute (CLSI) defines a single blood culture set as the combination of blood culture bottles into which a single blood specimen is inoculated. For adult patients, this generally equates to one aerobic and one anaerobic bottle.[6] It is recommended that two sets of blood cultures (total of four bottles), each containing 20 – 30 mL of blood and drawn from separate sites are obtained in adults with a suspicion for a bloodstream infection (BSI) in order to enhance interpretation of results and limit the likelihood of interpreting a contaminant as a true pathogen.[5]

In the context of blood cultures, a contaminant is a microorganism isolated from a blood culture that was introduced into the culture during specimen collection or processing and not pathogenic for the patient from whom blood was collected.[6,9] In contrast, a true pathogen is a microorganism isolated from a blood culture that is responsible for clinical disease. It is estimated that 10% – 15% of all blood cultures collected grow an organism, and approximately half of these are considered contaminants (e.g., 5% – 7.5% of all blood cultures performed).[10-12] Therefore, significant opportunities exist to limit antibiotic exposure to patients with contaminated blood cultures.

### How Can Contaminants be Differentiated from True Pathogens?

Differentiating blood culture contaminants from true pathogens is paramount for optimal patient care. Unfortunately, no standardized consensus or definitive algorithm exists and clinicians use their judgement in determining a true BSI.[13] Prior studies have shown independent predictors of bacteremia (caused by true pathogens) included time to culture positivity, presence of multiple positive cultures, and organism identity.[14,15] In recent years, however, the applicability of time to positivity has fallen out of favor due to the introduction of new microbiology laboratory testing methods.[16,17] Taking primary literature and expert opinion into account, we believe the following factors, in combination with the patient's clinical status, are most important to consider to differentiate true pathogens from possible contaminants:[14-17]

1. **Pathogen identity**
2. **The number of positive blood culture bottles relative to the total number collected**
3. **Whether or not each blood culture set was collected from a separate site or venipuncture**

## 1. Pathogen Identity

In general, most common microorganisms can be classified into two groups: 1) true pathogens, and 2) possible contaminants. True pathogens are microorganisms that, when isolated from even a single blood culture bottle, should always prompt further workup and treatment. In contrast, possible contaminants are typically skin flora. These pathogens do have the capacity to cause disease is certain scenarios such as infection of invasive devices (e.g. central venous lines, prosthetic heart valves) and procedures. However, they are more often recovered from blood cultures when introduced inadvertently during specimen collection or processing. **Tables 1 & 2** highlight examples of true pathogens and possible skin flora contaminants.[5,9,10]

One pathogen that may cause confusion is *S. lugdunensis.* Unlike other coagulase-negative staphylococci, *S. lugdunensis* often causes severe clinical disease resembling infections caused by *S. aureus.* Several factors contribute to the pathogenesis of this organism, including increased adherence factors, a greater capacity to form biofilms, and the ability to utilize host hemoglobin as an iron source.[18] Ultimately, isolation of *S. lugdunensis* from a blood culture should prompt treatment and a thorough workup to rule out complications.

**Table 1.** True pathogens that should prompt further workup and treatment[5,9,10]

| True Pathogens |
|---|
| *Staphylococcus aureus* |
| *Staphylococcus lugdunensis (a type of coagulase-negative staphylococcus)* |
| Group A Strep (e.g., *Streptococcus pyogenes*) |
| *Streptococcus pneumoniae* |
| *Pseudomonas aeruginosa* |
| Enterobacteriaceae (e.g., *E. coli* and *Klebsiella spp.*) |
| *Haemophilus influenzae* |
| *Candida spp.* |

**Table 2.** Possible contaminants[5,9,10]

| Possible Contaminants |
|---|
| Coagulase-negative staphylococci (CoNS) other than *S. lugdunensis* |
| *Cutibacterium acnes (formerly Propionobacterium)* |
| *Corynebacterium spp.* and other diptheroids |
| *Bacillus spp.* (other than *B. anthracis*) |
| *Micrococcus spp.* |
| Viridans group streptococci |

## 2. Number of Positive Blood Cultures

The number of positive blood culture bottles/sets relative to the total number collected is also an important factor to consider.[10,11] Patients with contaminated blood cultures often have only one positive blood culture bottle/set when two or more sets are collected, and the probability of recovering the same contaminant organism in two culture sets is low.[5,11,17] For example, in institutions with blood culture contamination rates of 3%, the probability of recovering the same possible contaminant in 2 sets is less than 1 in 1000 or < 0.1%.[17] Unfortunately, if only one set is sent for analysis, it is difficult to differentiate pathogens from contaminants. This limitation is one of the driving factors behind the CLSI's recommendation to always send at least two blood culture sets for analysis.[6] Infection preventionists also use the number of positive cultures in surveillance definitions to help determine central line associated BSI events.[19]

## 3. Collection Site

When differentiating true pathogens from possible contaminants, it is also important to consider whether or not each blood culture set was collected from a separate site. Contaminants are most often introduced during specimen collection; therefore, the likelihood of contamination is much less if the same organism is isolated from blood culture sets collected from separate sites. For example, a patient with infectious symptoms that has a possible contaminant (e.g., coagulase-negative *Staphylococcus spp.*) growing in 2/2 blood culture sets collected from separate sites should receive empiric treatment and further workup. In contrast, it may be appropriate to discontinue antibiotics, request repeat

cultures, and actively monitor a clinically-stable patient with 2/2 blood culture sets positive for a possible contaminant that were collected from the same site. Each blood culture specimen should be appropriately labeled with the patient's unique identification, site of venipuncture, date and time of collection, and the specimen number (e.g., 1 of 2, etc.).

**Table 3** provides some scenarios for interpreting blood culture results on the basis of the factors discussed above, which are readily available to clinicians.

## Take Home Points

- Contaminated blood cultures are common and associated with negative patient outcomes.
- Antimicrobial stewardship programs can reduce inappropriate treatment by assisting clinicians in identifying true pathogens and possible contaminants.
- *S. aureus*, *S. lugdunensis*, *P. aeruginosa,* other Gram-negative rods, and *Candida spp*. recovered from blood cultures should never be ignored (see Table 1).
- We recommend DASON hospitals follow best practices for collecting, handling, processing, and interpreting blood cultures in order to reduce blood culture contamination rates.

**Table 3.** Example blood culture algorithm for possible contaminants[13]

| Pathogen Identity | Number of Blood Culture Sets Collected + Collection Site | Number of Positive Cultures | Interpretation |
|---|---|---|---|
| **Possible contaminant (e.g., CoNS)** | 1 set obtained | 1 of 1 set positive | Limited evaluation, contamination or infection possible; additional clinical workup warranted |
| | ≥ 2 sets obtained from same or separate sites | 1 of 2 sets positive | Probable contamination |
| | ≥ 2 sets obtained from same site | 2 of 2 sets positive | Likely contamination; however, additional clinical workup warranted |
| | ≥ 2 sets obtained from separate sites | 2 of 2 sets positive | Possible infection; however, additional clinical workup warranted |
| **True pathogen (e.g., *S. aureus* or *S. lugdunensis*)** | 1 set obtained | 1 of 1 set positive | Likely infection; empiric therapy and additional clinical workup warranted |
| | ≥ 2 sets obtained from same or separate sites | 1 of 2 sets positive | |
| | ≥ 2 sets obtained from same or separate sites | 2 of 2 sets positive | |

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