Blood Cultures: An Overview

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One of the most important functions of the clinical microbiology laboratory is the detection, isolation, identification and antimicrobial susceptibility testing of microorganisms causing septicemia. The importance of this function is underscored by the correlation between appropriateness of antimicrobial therapy and outcome of the septic episode. Although many factors influence the initial and often empirical selection of an antimicrobial agent, such as underlying diseases or conditions, immune status and probable source of infection, a successful outcome is enhanced by use of antimicrobial agents to which the microorganism causing the septicemia is susceptible. Thus, it behooves the microbiologist to select the optimal procedures for rapid detection and isolation of the etiologic agent.

Much has been written about blood culture systems over the past 20 years. Whereas inadequate microbiology was the most frequent cause of culture-negative infective endocarditis until the middle to late 1960s, the prior administration of antimicrobial agents became the most frequent cause of this problem thereafter (1–3).

Some diversification of blood culture systems has occurred since the 1960s. Commercially prepared vacuum blood culture bottles have largely replaced "home-made" blood culture bottles. In the process manufacturing practices have provided a variety of media which in the vacuum bottle retain a redox potential that is highly favorable to the growth of many anaerobic bacteria. Sodium polyanetholesulfonate (SPS) has become a routine additive to blood culture media and provides not only anticoagulant but also antiphagocytic and anticomplementary properties to the media. Many blood culture bottles contain an atmosphere consisting of an inert gas and carbon dioxide. Numerous physiochemical approaches to growth detection have been devised; however, the only one that reached the marketplace was one based initially upon the radiometric detection of $^{14}\text{CO}_2$ and more recently one that is based on infrared photometric detection of CO$_2$.

Other approaches remain under development. Biphasic medium blood culture bottles were originally designed for the isolation of Brucella from blood (4) and were subsequently adapted for the isolation of bacteria and fungi from blood (5–7); however, it was not until the invention of a simple chamber attachment that biphasic blood culture bottle systems became commercially available (8, 9). Although initially designed for the isolation of tubercle bacilli from blood (10), lysis concentration techniques remained impractical for clinical laboratory use until the 1980s (11).

Given the variety of blood culture systems that are currently available, what are some of the unresolved problems and what are some of the issues surrounding the process of detection of septicemia?

First, there are a number of issues related to collection of blood for culture. In most instances, and particularly in those associated with an undrained focus of infection, bacteremia and candidemia are intermittent. Since microorganisms are not constantly in the blood stream, the sensitivity of a single blood culture is between 80 and 90%. Thus, it is recommended that more than a single blood culture be performed (12). How many blood cultures should be performed? I remember a case of viridans streptococcal endocarditis for whom enthusiasm to establish the diagnosis and oversight of previously ordered cultures by successive consultants led to the performance of 21 blood cultures within the first 24 hours of hospitalization! Every single bottle from every single set of cultures yielded a viridans streptococcus. This bit of diagnostic overkill, incidentally, led to a cumulative loss of a unit of blood. Published data demonstrate that it is rarely necessary to perform more than two or three blood cultures per septic episode or case of infective endocarditis (1, 13). Since prior antimicrobial therapy adversely affects the yield of bacteria from patients with infective endocarditis, it may be prudent in such instances to perform two to three separate blood cultures on each of two days (Figure 1). If blood cultures remain negative after a period of seven days, it may be necessary to consider other pathogens, such as Legionella, Coxiella or filamentous fungi. The diagnosis of Legionella and Coxiella endocarditis is ordinarily made serologically, although subcultures of broth media and culture of lysed concentrate on buffered charcoal yeast extract agar have resulted in the isolation of Legionella in such cases (14). The diagnosis of filamentous fungal endocarditis is rarely made by blood culture, usually being made histologically or by culture of valve tissue (15). Although
often cited as causes of culture-negative infective endocarditis, *Haemophilus, Actinobacillus, Cardio-
bacterium, Eikenella* and *Kingella* (the so-called "HACEK" group) are usually detected within seven
days on incubation of blood cultures. In my ex-
perience with 30 such cases, only one case would
have been missed had all blood cultures been rou-
tinely discarded in seven days, and in that particular
case all signs and symptoms were strongly suggestive
of endocarditis and blood cultures became positive
on the eighth day of incubation (unpublished observa-
tions).

A second issue today relates to the source of blood to
be cultured. With the increasing number of patients
with temporary or permanent intravascular lines that
often serve as the major access site to blood for a
variety of therapeutic and monitoring purposes,
there has been an increase in blood collection for
culture from such sites. Moreover, some investigators
promote the concurrent collection of blood from
peripheral venous and central lines for quantitative
culture on the basis that if the number of colonies
from the central line blood culture is 5 to 10 times
that from the peripheral venous blood culture, line-
related infection can be established (16–18). None-
theless, contamination of blood drawn through a
three-way stopcock on an arterial line frequently
yields a small number of colonies of coagulase-
negative staphylococci so that caution must be
observed when the results of such cultures are reported
by the laboratory.

A third issue is the volume of blood to be cultured.
More than one blood culture is obtained to increase
the probability of detecting intermittent bacteremia
or candidemia. A large volume of blood per culture
is obtained because the number of bacteria or yeasts
per milliliter of blood, at least in adults, is small. In
many cases bacteremia and candidemia is associated
with < 1 CFU/ml of blood (11, 19). The difference
in yield between cultures of 10 and 20 ml of blood
is as high as 40% (20). Volume of blood per culture,
therefore, is the major determinant of yield, regardless
of what blood culture system is used. Lack of atten-
tion to this important variable is one of the most
common mistakes made by microbiologists in formu-
lating blood culture procedures and by industry in
designing new blood culture systems.

The fourth major issue is the selection of blood
culture systems. There is no single blood culture
bottle or device that is suitable for all purposes. If
vacuum bottles are used in which the medium has a
low redox potential, it should be apparent that
strictly aerobic bacteria and yeasts will fail to grow.
Conversely, anaerobic bacteria will be detected
significantly less frequently if only vented or aerobic
bottles are used. The possible presence of these
microorganisms with mutually exclusive atmospheric
growth requirements should make it obvious that
both aerobic and anaerobic blood culture bottles are
necessary, however it is interesting to note that many
facultatively anaerobic bacteria are more frequently
isolated from aerobic than anaerobic atmospheres of