

ASTar provides highly accurate results up to 16 h after positivity of blood culture flasks

Timing is vital in the targeted treatment of bloodstream infections. The majority of EU labs performing antimicrobial susceptibility testing (AST) operate a single shift versus a 24 h microbiology service. While 24h-open labs can perform Gram staining on positive blood cultures and more complex microbiological analyses around the clock, single shift labs have a limited timeframe to perform such tests. ASTar® BC G– Kit provides highly accurate AST results up to 16 h after positivity of Gram-negative blood culture flasks. This minimizes the need for collecting extra samples, reduces hands-on time, and decreases overall time to the start of adequate antimicrobial treatment.

Introduction

Current workflows for diagnosis of bloodstream infections in EU clinical microbiology laboratories are based on sub-culturing microbes from positive blood cultures followed by identification, often using semiautomated systems, molecular methods, or MALDI-TOF mass spectrometry (MS) (1). Subsequent susceptibility testing is done by overnight disc diffusion or semiautomated systems. In practice, this means that information to support both guided treatment and de-escalation of empirical broad-spectrum antimicrobials is achieved at the earliest 48 h after blood draw, although workflows may differ between laboratories (2). During recent years, techniques for rapid identification (ID) of bacteria have become available and are increasingly adopted by microbiology labs. Combining the development of rapid ID with antimicrobial stewardship has already shortened the time to optimal treat-

ment of bloodstream infections (2-4). However, for accurate and targeted therapy, not only rapid ID, but also rapid phenotypic AST is needed. With this in mind, the ASTar system was developed to provide rapid, phenotypic AST that enables the timely administration of adequate antimicrobials.

ASTar – rapid AST results directly from clinical samples

ASTar is a new, fully automated system for rapid AST. The proprietary AST technology is based on broth microdilution (BMD), optimized for high sensitivity and short time-to-result, delivering phenotypic AST with true minimum inhibitory concentration (MIC) results in approximately 6 h.

Scenario for daytime open clinical microbiology laboratories

During the 12h time period the lab is not operational, samples that have turned positive may be missed. Previously, this would require taking additional blood samples and repetition of subculturing steps in the lab. It is estimated that up to 20% of all blood culture flasks (BCFs) that turn positive during 24h could be missed in day-open laboratories.

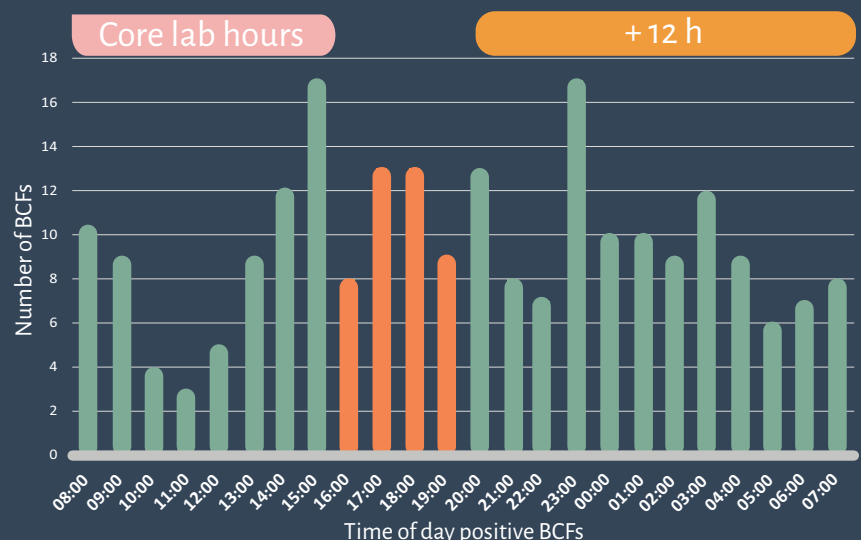


Fig1. Timing in the day of blood culture flasks turning positive for day-open clinical microbiology labs (5).

Table 1. Positive blood culture bottles can be stored at room temperature or remain in the blood culture cabinet for up to 16h before they are run on the ASTar Instrument using the BC G– Kit.

Condition compared to reference	MIC values within +/- 1 of modal values of reference/ Total number of MIC values	Percent success rate
16 h room temperature	155/165	93,9%
16 h blood culture cabinet	157/165	95,2%

The first application is Gram-negative bloodstream infections, with AST directly from positive blood cultures.

Scenario for daytime-open labs

In daytime-open clinical microbiology laboratories, another factor influencing the workflow efficiency, is the timing of taking blood samples, and subsequently of blood culture flasks turning positive. For blood culturing in hospital wards, most samples are collected in the morning after the clinical rounds. Given an average time to positivity of 10–16 h, most will turn positive at night.

At the emergency department, blood cultures are drawn around the clock as patients present with signs of infection of unknown origin. Those cultures turn positive more equally distributed around the clock. In summary, around 50 to 65% of the blood cultures will become positive outside lab hours in a standard single shift lab (see Figure 1).

ASTar clinical performance

In this study we evaluated the potential of the ASTar Instrument and BC G– Kit to provide accurate results in a time-after-positivity challenge and under different temperature conditions. To this end, blood culture flasks, (BACTEC Plus Aerobic, glass) were loaded with recommended blood volumes and seeded with one of four different bacterial species, *E. coli*, *K. pneumoniae*, *P. aeruginosa* or *H. influenzae*, and incubated until positivity. These blood cultures for Gram-negative bacteria were then analyzed ≥ 16 h after positivity. For reference values, positive flasks were run on the ASTar Instrument within 1

h after positivity. In addition, different temperatures for storage of positive BCFs were evaluated. One batch was stored at room temperature (approx. 25 °C), and another batch was stored in the blood culture cabinet (35 \pm 2 °C). Each test setup was repeated three times per species.

AST results

For the four organisms tested in triplicate against the ASTar BC G– antimicrobial panel, the AST results were shown to be stable up to 16 h from positivity of the blood culture bottles. Both storage conditions of the positive BCFs rendered stable results.

Conclusion

The ASTar Instrument and BC G– Kit can potentially prevent previously missed positive blood culture flasks, by extending the time window of analysis start after BCFs turn positive. Running BCFs up to 16 h after positivity will allow for around-the-clock inclusion of all positive blood samples, regardless of timing. This will improve workflow efficiency in single shift microbiology labs and minimize time to the start of adequate antimicrobial treatment.

References

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Q: Thinking of your laboratory workflow and organisation, what are the advantages of an AST technology that can analyze clinical blood culture samples within 16 h from positivity?

A: In many diagnostic laboratories positive blood cultures are still processed during the opening hours, while any blood culture turning positive outside the opening hours are processed on the next morning. Under these circumstances, some positive blood cultures cannot be processed with rapid AST systems which require a relatively short time (a few hours) between positivity and processing. The availability of a rapid AST system that provides reliable results up to 16 h after positivity of a blood culture, therefore, is a definite advantage for laboratories that cannot process positive blood cultures on a 24/7 basis.

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