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A Rapid Test for Microbial Identification in Patients With Suspected Sepsis



Image courtesy of BioFire Diagnostics, LLC

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Summary

- The FilmArray Blood Culture Identification (FA-BCID) panel is a multiplex polymerase chain reaction–based rapid diagnostic test that can detect 24 sepsis-related pathogens (bacteria and yeast) and three antimicrobial resistance genes in patients with suspected sepsis.
- An initial blood culture is still required, as the FA-BCID panel must be performed on blood cultures that have tested positive (indicating initial microbial growth).
- The FA-BCID panel can identify specific pathogens from positive blood cultures with a turnaround time of approximately one hour; this is significantly faster than the time required to grow a full blood culture to identify pathogens.
- The sensitivity and specificity of the FA-BCID panel are well established for organisms included in the panel; however, its primary limitation from a diagnostic standpoint is an inability to detect other pathogens not included in its panel.
- Used along with antimicrobial stewardship programs, the FA-BCID panel may improve patient outcomes by, for example, reducing the time it takes to receive appropriate antimicrobial therapy and shortening hospital stays.
- No comprehensive economic evaluations were identified.

Background

The incidence of sepsis is rising and is an increasing concern, both in terms of morbidity and mortality as well as cost to the health care system.¹⁻⁴ Recently, the definitions and clinical criteria for sepsis and septic shock have been redefined in light of a changing and rapidly evolving understanding of the condition's underlying pathobiology.³ A Task Force convened by the Society of Critical Care Medicine and the European Society of Intensive

Care Medicine now defines these conditions as follows:³

- Sepsis — a “life-threatening organ dysfunction caused by a dysregulated host response to infection.”
- Septic shock — “a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.”

Symptoms of sepsis include fever, chills, confusion or disorientation, shortness of breath, an elevated heart rate, low blood pressure, high blood sugar levels, swelling, and other signs of infection at the original site/source.^{5,6} Sepsis is suspected clinically when both of the following are present:

- The patient has a suspected infection (an infection originating from elsewhere in the body — such as pneumonia, influenza, or a urinary tract infection — can often progress into the bloodstream).⁷
- The patient shows signs of organ dysfunction, as demonstrated by an increase of two or more points on their Sequential Organ Failure Assessment score.^{3,8}

Testing for a bloodstream infection — and identifying the specific pathogen(s) responsible for it — is a key part of managing a patient with suspected sepsis.⁹

“The FA-BCID panel is currently indicated as an additional diagnostic tool for use after the presence of a bloodstream infection has been identified with a blood culture — it is not intended for independent use.”

The gold standard for diagnosing a bloodstream infection is a blood culture.^{5,9} However, the primary limitation of relying on blood cultures alone is the long turnaround time for pathogen identification. (It typically takes 24 hours to 72 hours or more to obtain the test results).¹⁰⁻¹² This, in turn, leads to a delay in providing optimal treatment (targeted antimicrobial therapy) for patients with sepsis. Rapid diagnostic tests are being developed to address this limitation.⁵

The Technology

The FilmArray Blood Culture Identification (FA-BCID) panel (BioFire Diagnostics, LLC, Salt Lake City, and bioMérieux Canada, Inc., Saint-Laurent, QC) is a multiplex polymerase chain reaction

(PCR)-based rapid diagnostic test that is intended for rapid microbial identification in patients with suspected sepsis.^{13,14}

The proposed benefits of the FA-BCID panel include:¹⁵⁻¹⁸

- a faster time to pathogen identification for patients with suspected sepsis
- reduced time to appropriate antimicrobial therapy.

The FA-BCID panel is currently indicated as an additional diagnostic tool for use after the presence of a bloodstream infection has been identified with a blood culture — it is not intended for independent use.¹⁹ Once the growth of microorganisms has been observed in a blood culture, the positive culture can then be tested using the FA-BCID panel. This panel can detect 24 microorganisms (eight gram-positive bacteria, 11 gram-negative bacteria, and five *Candida* species) and three antibiotic-resistance genes.¹³

The FA-BCID panel, by applying PCR-based techniques to blood cultures as soon as they signal positive (at the initial stages of microbial growth), may save time.¹³ Pathogens covered by the FA-BCID panel can be identified in approximately one hour, which is faster than the 24 to 72 hours required for full blood culture results.¹³ However, to diagnose any pathogen(s) not covered by the FA-BCID panel, it is still necessary to grow the full blood culture.¹⁹

Using multiplex PCR-based techniques (which amplify and detect multiple genetic sequences of interest in a single experiment), the FA-BCID assay detects short sequences of RNA and DNA from microorganisms and antibiotic-resistance genes, and matches these to its database.¹³ The FA-BCID technology consists of:²⁰

- an analyzer (a one-time purchase re-used for all tests)
- FA-BCID panels/tests (which contain the reagents to which the positive blood culture sample is added; a new panel is needed each time the test is run)
- a desktop computer with pre-loaded software to interpret the results by matching genes to a database.²⁰

Results are automatically reported approximately one hour later.¹³

Availability

The FA-BCID panel is commercially available in Canada, the US, and elsewhere.^{14,19,21} The panel was approved by Health Canada in November 2015,¹⁴ and the FDA granted it a 510(k) approval in March 2016.²¹

Cost

The Canadian cost to purchase the FilmArray analyzer (with accompanying desktop computer and software) is \$50,000. Each FA-BCID panel (test) is \$180.00. No other supplies are needed (François Turgeon, Senior Manager, Clinical Marketing, bioMérieux Canada, Inc., Saint-Laurent, QC: personal communication, 2017 August 25).

Current Practice

The Surviving Sepsis Campaign: International Guidelines for the Management of Sepsis and Septic Shock were updated in 2016.⁹ These evidence-based guidelines form the current recommendations for the diagnosis and management of sepsis.⁹

“Patients with suspected sepsis might benefit from the FA-BCID panel if it results in the faster identification of selected pathogens and, in turn, reduces the time until they receive appropriate antimicrobial therapy.”

The guidelines state that patients with a suspected bloodstream infection should receive a blood culture.^{5,9} The blood sample to be used for the culture should be obtained prior to starting antimicrobial therapy to prevent the treatment from killing the pathogen(s) responsible for the infection before they can be identified.^{5,9,10} Positive blood cultures (those showing initial microbial growth) are then sent for further testing to identify specific pathogen(s), and for antimicrobial susceptibility testing to determine the most appropriate antimicrobial therapy.⁵

Following initial sampling, patients showing clinical signs of sepsis (organ dysfunction) should be started proactively on intravenous broad-spectrum antimicrobial agents to reduce the risk of death (the mortality rate of sepsis increases by 7.6% for each hour of delay in receiving treatment).⁵ Longer delays in treatment have been linked to adverse effects such as hospital-acquired infections, organ damage, and longer hospital stays.⁹

Once the pathogen causing the infection is identified and antimicrobial susceptibility determined, the treating physician can provide the patient with therapy specifically targeted to the pathogen.^{5,9}

Who Might Benefit?

The FA-BCID panel is intended for patients with suspected sepsis.²² In 2008-2009 more than 30,000 Canadians (from all provinces excluding Quebec) were hospitalized with sepsis and more than 9,000 deaths (about 30% of all patients) were attributed to the condition.² Mortality rate estimates for sepsis range from 18% to greater than 50% around the world.^{2,23-25} Patients with sepsis spend an average of nine additional days in hospital compared with those without.^{2,26} In 2008-2009, sepsis represented 10.9% of all in-hospital deaths in Canada (all provinces excluding Quebec).²

Risk factors for sepsis include age (infants and the elderly are most affected), male sex, non-Caucasian ethnicity, having had a recent health care intervention (for example, placement of a catheter or central venous line, or surgery), and the presence of comorbidities (especially those that compromise the immune system, such as diabetes, HIV/AIDS, or cancer).^{1,5}

Patients with suspected sepsis might benefit from the FA-BCID panel if it results in the faster identification of selected pathogens and, in turn, reduces the time until they receive appropriate antimicrobial therapy.²²

The Evidence

We identified 22 studies of the FA-BCID panel.^{15-18,27-44} In most studies,^{15-18,27-29,31,32,35,36,38,39,41-44} the FA-BCID panel was compared with the diagnostic gold standard (blood culture) for patients with suspected sepsis. Two studies compared the FA-BCID panel with other rapid diagnostic tests – Verigene (Luminex

Corporation, Toronto) and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).^{34,37,40} One study used a combination of MALDI-TOF MS and the FA-BCID panel and compared this with blood culture.³⁰ The evidence focuses on the following seven outcomes:

- test performance and reliability
- sepsis-related mortality and potential reduction
- time to appropriate therapy
- hospital length of stay
- changes in patient management
- usability in remote settings
- cost evaluations.

Test Performance and Reliability of the FA-BCID Panel

Salimnia et al. performed an eight-centre, manufacturer-funded trial, which is the largest single study of the FA-BCID panel to date.³¹ A total of 2,207 samples showing microbial growth were tested, including 1,568 prospectively collected clinical samples left over from patients who had undergone blood culture testing and 639 samples seeded with a known microorganism to ensure a sufficient number of samples with each microorganism of interest for analysis. The FA-BCID panel detected at least one organism in 1,382 (88.1%) of the clinical samples, and multiple organisms in 81 (5.16%) of the clinical samples. The combined results for the accuracy of the FA-BCID panel for the clinical samples (calculated as sensitivity [the ability of the test to correctly identify patients with an infection] and specificity [the ability of the test to correctly identify people without an infection]) and agreement of the FA-BCID panel for the seeded samples (calculated as positive per cent agreement and negative per cent agreement, used when comparing a new test with a non-reference standard, in this case known samples) for organisms included in the panel are summarized in Table 1.

Table 1: Sensitivities and Specificities for Organisms and Antimicrobial Resistance Genes Included in the FA-BCID Panel³¹

Type of Organism or Antimicrobial Resistance Gene	Sensitivity/PPA	Specificity/NPA
Gram-positive bacteria	97.3%	99.8%
Gram-negative bacteria	98.1%	99.9%
<i>Candida</i> species	99.2%	99.9%
<i>mecA</i>	98.4%	98.3%
<i>vanA/B</i>	100.0%	100.0%
<i>blaKPC</i>	100.0%	100.0%

blaKPC = *Klebsiella pneumoniae* carbapenemase; *mecA* = methicillin-resistant; NPA = negative per cent agreement; PPA = positive per cent agreement; *vanA/B* = vancomycin A/B.

We identified eight smaller, single-centre studies that also evaluated the performance of the FA-BCID panel.^{18,27,34-39} The findings were similar to Salimnia et al. for organisms included in the panel. The primary reason for missed diagnoses was the presence of organisms not included in the panel.

In addition to assessing diagnostic accuracy, Altun et al. performed a small study of five blood cultures over four weeks to assess the reproducibility and stability of the FA-BCID panel test results.³⁸ Results for the repeat tests were identical to the initial test results.

Sepsis-Related Mortality

Two studies^{28,32} and three poster presentations⁴²⁻⁴⁴ reported no difference in mortality with the introduction of the FA-BCID panel, noting trends toward reduced mortality with use of the FA-BCID panel.

Time to Appropriate Therapy

MacVane et al. evaluated the impact of the FA-BCID panel in a setting with an already-established antimicrobial stewardship program.¹⁷ The study included 364 patients: 115 formed the control group (an historical group diagnosed using standard blood culture), 104 received the already-established antimicrobial stewardship program alone, and 145 patients

received testing with the FA-BCID panel in addition to the program. Only patients with organisms included in the FA-BCID panel were included for analysis. The time to organism identification in the FA-BCID group decreased by 37 hours compared with the antimicrobial stewardship program group and 40 hours compared with the control group. The time to appropriate therapy in the FA-BCID group decreased by eight hours compared with the antimicrobial stewardship program group and 10 hours compared with the control group.

Messacar et al. evaluated the impact of the FA-BCID panel plus an antimicrobial stewardship program on the time to optimal antimicrobial therapy for pediatric patients.¹⁸ The study included 300 pediatric patients: 200 in the pre-intervention control group and 100 in the post-intervention group. The median time to optimal antimicrobial therapy decreased by 33.5 hours with use of the FA-BCID panel plus the antimicrobial stewardship program.

Hospital Length of Stay

Two single-centre studies found that using the FA-BCID panel decreased hospital length of stay when compared with blood culture alone.^{15,32}

Pardo et al. assessed the effectiveness of the FA-BCID panel for patients with gram-positive cocci and *Candida* (fungal) infections.³² Eighty-four patients who received the FA-BCID panel were compared with 252 historical controls. The median length of stay in the FA-BCID panel group was 0.6 days shorter than the control group. The authors largely attributed the decreased length of stay to the detection of likely contaminants (i.e., false positives due to coagulase-negative *Staphylococcus aureus* [CoNS] contamination), allowing patients who did not have actual bloodstream infections or sepsis to be discharged earlier. (However, this study evaluated only CoNS contamination, and did not consider other possible contaminants such as *Propionibacterium* or *Corynebacterium* species.)

Ray et al. assessed whether FA-BCID panel results led to changes in length of stay at a tertiary referral pediatric hospital over a period of six months.¹⁵ The FA-BCID panel was performed on 117 positive blood cultures from patients with a median age of 1.5 years. A total of 10 children were discharged from the hospital earlier, and a total of 14 hospital bed days were saved. In all cases, the authors reported that early discharge

was the result of the detection of likely contaminants (i.e., false positives). However, in two of the 10 cases, patients were subsequently recalled when blood culture results became available and the cultures grew additional organisms that were not initially detected by the FA-BCID panel.

Three poster presentations also considered the impact of the FA-BCID panel on hospital length of stay.^{41,42,44} The studies found no difference in length of stay after FA-BCID implementation compared with patients pre-intervention, but trends toward reductions in hospital length of stay of 0.5 days,⁴⁴ 1.6 days,⁴² and 3.1 days⁴¹ were noted.

Changes in Patient Management

Ray et al. assessed whether use of the FA-BCID panel led to changes in clinical management at a tertiary referral pediatric hospital over a period of six months.¹⁵ The FA-BCID panel was performed on 117 positive blood cultures and, in 63 cases (54%), the FA-BCID results were reported to have changed clinical management. Initiation or escalation of antimicrobial therapy occurred in 23 cases (19%), while de-escalation or cessation of broad-spectrum agents occurred in 29 cases (25%).

Messacar et al. also assessed changes in patient management and found care was changed (narrowed or expanded use of antimicrobials or avoided return visits) in 73% of cases, as reported by health care providers.¹⁸

No studies reported on whether changes in patient management led to changes in health outcomes.

Usability by Non-Expert Staff and in Remote Settings

Two studies evaluated the use of the FA-BCID panel in more remote settings with non-expert staff.^{29,33}

McCoy et al. compared use of the FA-BCID panel performed by non-expert staff with blood cultures performed by skilled microbiologists.²⁹ The purpose was to evaluate the utility of the FA-BCID panel in settings with limited expert staffing. Out of 200 samples:

- All organisms in 172 (86%) of the samples were correctly identified by non-expert staff using the FA-BCID panel.

- Organisms in 20 (10%) of the samples were not covered by the FA-BCID panel and were therefore not identified (but were identified by blood culture).
- Results for seven (3.5%) of the samples had a discrepancy between the FA-BCID panel and blood culture that was attributed to the misidentification of two organisms in two samples and five samples where the blood culture did not produce the organism detected by FA-BCID.
- Results for one (0.5%) of the samples was deemed invalid and eliminated from the study.

Non-expert staff, who received less than 10 minutes of training on the system, reported the FA-BCID panel was user-friendly. It was noted that it may be particularly beneficial in laboratories with limited staffing or technical expertise.

Inglis et al. evaluated Western Australia's use of the FA-BCID panel in smaller regional hospitals, where blood culture results are often delayed because samples must be processed in a central lab located several hundred kilometres away, and in a large teaching hospital, where blood cultures can be processed on site.³³ A total of 149 consecutive blood samples from 143 patients were assessed (89 positive blood samples from 86 patients in the teaching hospital and 60 positive blood samples from 57 patients in smaller regional hospitals). The results were as follows:

- Eighteen of the 34 microorganisms (53%) identified by blood cultures from samples in the teaching hospital were included on the FA-BCID panel.
- Twenty of the 23 microorganisms (87%) identified by blood cultures from samples in the regional hospitals were included on the FA-BCID.
- The FA-BCID panel correctly identified 85% of single-pathogen bloodstream infections in the teaching hospital.
- The FA-BCID panel correctly identified 100% of single-pathogen bloodstream infections in the smaller regional hospitals.

The authors noted that regional hospitals tend to encounter a smaller range of pathogens, thus improving the relative diagnostic precision of the FA-BCID panel in these settings.

Although not designed to evaluate the impact of using FA-BCID on the time needed to identify sources of infection, the authors noted that using FA-BCID reduced the time to identify blood culture isolates by more than 52 hours in the regional hospitals and that more research should be conducted to determine the clinical and economic impact of offering this type of rapid testing.

Cost Evaluations

We did not identify any formal cost-effectiveness studies of the FA-BCID panel. However, several studies have reported on costs associated with its use.^{17,28,32,41-43}

Pardo et al. evaluated the clinical and economic impact of simultaneously introducing rapid testing with the FA-BCID panel and an antimicrobial stewardship program for patients with gram-positive or *Candida* (fungal) infections.³² Eighty-four FA-BCID panel patients were compared with 252 historical controls. Use of the FA-BCID panel was found to save approximately US\$30,000 per 100 patients (attributed to savings from shortened length of stay and reduced pharmacy costs) compared with the control group even after accounting for additional costs in using the FA-BCID panel, such as the cost per test.

MacVane et al. evaluated the impact of the FA-BCID panel in a setting with an already-established antimicrobial stewardship program.¹⁷ No difference in total hospital costs was found when the FA-BCID panel was implemented when compared with a historical control group and a group of patients who received an antimicrobial stewardship program.

Another study by MacVane et al. evaluated use of the FA-BCID panel plus an antimicrobial stewardship program specifically for patients with vancomycin-resistant enterococcal bloodstream infections (sample size of 68).²⁸ No difference in total hospital costs was found compared with patients diagnosed using conventional methods.

Three poster presentations also found no difference in costs with use of the FA-BCID.⁴¹⁻⁴³

Safety

None of the studies of the FA-BCID panel reported any safety concerns with its use.

“The FA-BCID panel is one of several rapid diagnostic tests that have been developed for faster identification of sepsis-related pathogens.”

The FDA’s 510(k) decision summary noted some limitations of the FA-BCID panel, including the following:¹⁹

- The absence of detection of the three antimicrobial resistance genes does not necessarily equate to antimicrobial susceptibility, as there are multiple mechanisms of resistance to methicillin, vancomycin, and carbapenems, not all of which are detectable by the FA-BCID panel.⁴⁵
- The absence of pathogen detection altogether by the FA-BCID panel does not exclude the possibility of a bloodstream infection.
- The identification of one (or more) pathogen(s) by the FA-BCID panel does not exclude the possibility of additional organism(s) that may be present in polymicrobial cultures.

For these reasons, the FA-BCID panel is intended as an adjunct diagnostic tool, to be used alongside blood culture.¹⁹

Concurrent Developments

Rapid Diagnostic Tests for Sepsis

The FA-BCID panel is one of several rapid diagnostic tests that have been developed for faster identification of sepsis-related pathogens.

One of the leading concurrent developments, MALDI-TOF MS, is used in many Canadian hospitals. Two MALDI-TOF MS systems are available in Canada: the VITEK MS (bioMérieux), and the Flex and Microflex series (Bruker Daltonics Ltd., East Milton, ON).⁴⁶ Advantages of MALDI-TOF MS include its large database for species and genus identification, low cost per sample analyzed, relatively simple procedure for use, fast turnaround time, and ability to detect pathogens at earlier stages of growth (i.e., after only a few hours of incubation).^{10,47} The main disadvantage of MALDI-TOF MS is that it does not currently test for antimicrobial

resistance. However, this is an active area of research, and in the future the technology may be expanded to include the detection of antimicrobial resistance.^{10,48,49}

Another noteworthy development is Verigene.⁴⁸ It is a microarray-based system with two separate panels: the gram-positive panel includes 13 species or genus targets and three resistance genes, and the gram-negative panel includes nine species or genus targets and six resistance markers.¹⁰ Its turnaround time is approximately 2.5 hours.¹⁰ An advantage of Verigene is that it has a greater capacity to detect antimicrobial resistance than other currently available rapid diagnostic tests. This allows earlier initiation or escalation of therapy if a multi-drug resistant organism is detected, as well as earlier use of contact isolation protocols for patients found to have methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci.^{10,48} Limitations of Verigene are that in samples with more than one microorganism the test cannot determine which organism(s) are the source of antimicrobial resistant genes, and it also cannot detect fungal targets.¹⁰

In a direct comparison with conventional blood culture identification, both the FA-BCID panel and Verigene were found to provide accurate results in less time than conventional methods.³⁴

Other commercially available rapid diagnostic tests for sepsis include Prove-it Sepsis (Mobidiag, Espoo, Finland), VYOO (Analytik Jena AG, Jena, Germany), SepsiTTest (Molzymb GmbH & Co. KG, Bremen, Germany), Magicplex sepsis real-time (Seegene, Inc., Seoul, Korea), the LightCycler SeptiFast assay (Roche Diagnostics Canada, Laval, QC), the T2Candida Panel (with the upcoming release of the T2Bacteria Panel, making for the combined T2Sepsis Solution) (T2 Biosystems, Lexington, MA), the Xpert MRSA/SA BC assay (Cepheid, Sunnyvale, CA), and the recently FDA-cleared iCubate System (iCubate, Huntsville, AL).^{10,50-53}

Two systematic reviews and meta-analyses have compared rapid diagnostic tests for sepsis (such as PCR-based methods, MALDI-TOF MS, and peptide nucleic acid fluorescent in situ hybridization-based methods), with or without antimicrobial stewardship programs, with blood culture.^{54,55} Both found that the rapid tests had a positive impact on clinical outcomes for patients with sepsis, including reduced mortality, improved time to appropriate antimicrobial therapy, and decreased hospital length of stay.^{54,55} Of note, the effectiveness of rapid tests

was shown to be better when accompanied by antimicrobial stewardship programs (to ensure that a faster time to diagnosis was followed with appropriate changes in patient management).^{54,55}

Combined Interventions

Bookstaver et al. evaluated the effect of a “stewardship bundle” (antimicrobial stewardship plus rapid diagnostic testing) on appropriate antimicrobial therapy in gram-negative bloodstream infections.¹⁶ Following a pre-intervention phase to establish the proportion of patients receiving appropriate therapy, two phases of interventions were introduced sequentially: phase I interventions consisted of MALDI-TOF MS plus gram-negative bloodstream infection management guidelines and prospective stewardship review and feedback, and phase II consisted of all previously introduced interventions plus the FA-BCID panel. After implementing the bundle, appropriate therapy increased to 95% of patients, compared with 91% of patients in the pre-intervention phase. Using the bundle also decreased the time to de-escalation of broad-spectrum antibiotics (two days in phase I and one day in phase II compared with 2.8 days pre-intervention).

Fiori et al. conducted a study evaluating the impact of a bloodstream infection algorithm that combined MALDI-TOF MS plus the FA-BCID panel.³⁰ After a positive blood culture, samples were tested using the MALDI-TOF MS system for identification. If the MALDI-TOF MS results indicated a single source of infection, treatment was initiated. For MALDI-TOF MS samples indicating the presence of multiple microorganisms or producing unreliable results, the FA-BCID panel was then used to attempt identification. The combined use of MALDI-TOF MS and the FA-BCID panel correctly identified 97.7% of bloodstream infections – greater diagnostic accuracy than either test could have produced alone. The median time to pathogen identification was reduced by 22.3 hours compared with traditional blood culture methods.

Other FilmArray Analyzer Panels

In addition to the FA-BCID panel for sepsis, there are three other FilmArray panels available for other indications:²²

- **The FilmArray Meningitis/Encephalitis (ME) Panel** detects 14 target pathogens commonly responsible for central nervous system infections including bacteria, viruses, and yeast.

- **The FilmArray GI Panel** detects 22 target pathogens commonly responsible for gastrointestinal infections including bacteria, viruses, and parasites.
- **The FilmArray Respiratory Panel** detects 20 target pathogens commonly responsible for upper respiratory infections including bacteria and viruses.

Implementation Issues

Uptake

As of July 2017, four Canadian hospitals are using FilmArray analyzers (François Turgeon: personal communication, 2017 August).

Considerations for Rapid Diagnostic Tests for Sepsis

Factors to consider when evaluating the relative utility of different rapid diagnostic tests for sepsis include:

- the range of identifiable pathogens and resistance genes
- the turnaround time compared with other tests on the market
- the cost per test
- how easy or complex the test is to perform
- how it fits into hospital workflow.¹⁰

Very few studies have compared the FA-BCID panel with other rapid diagnostic tests.^{33,34,37,40} As a result, it is difficult to place the FA-BCID panel within the spectrum of available rapid diagnostic tests.

Many of the studies evaluating the FA-BCID panel combined use of the test with an antimicrobial stewardship program.^{16-18,28,32,36,41,42} This has been shown in systematic reviews and meta-analyses of other rapid diagnostic tests to further improve outcomes (by ensuring that rapid test results are translated into a faster time to appropriate antimicrobial therapy).^{54,55} The addition of antimicrobial stewardship programs may lead to other implementation considerations, such as staffing and establishing effective communication protocols, as well as related costs.

Final Remarks

The evidence to date suggests that the FA-BCID panel, particularly when combined with antimicrobial stewardship programs, may help improve patient care by allowing pathogens to be identified more quickly and by leading to the more appropriate use of antimicrobial agents.

The FA-BCID panel may also help improve antimicrobial stewardship by allowing more judicious use of high-potency, broad-spectrum antimicrobial agents based on individual patient's test results.

The specificity and sensitivity of the test have been well established, and the primary limitation of the FA-BCID panel from a diagnostic standpoint is its inability to detect organisms not included in the panel.

There is limited direct evidence on the ability of the FA-BCID panel to improve clinical outcomes (such as morbidity and mortality) or to reduce health care costs. Multi-centre controlled trials and a formal cost-effectiveness evaluation of the FA-BCID panel are still needed.

Methods

Literature Search Strategy

A peer-reviewed literature search was conducted using the following bibliographic databases: MEDLINE, Embase, PubMed, and the Cochrane Library (2017, Issue 5). Grey literature was identified by searching relevant sections of the Grey Matters checklist (<https://www.cadth.ca/grey-matters>). No methodological filters were applied. The search was limited to English-language documents published between January 1, 2012, and June 21, 2017. Regular alerts updated the search until project completion; only citations retrieved before August 8, 2017, were incorporated into the analysis. Conference abstracts were retrieved through a search of the Embase database limited to the last two years.

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