Clinical Bulletin: DxWound *mecA* Test

Description

Antibiotic resistance is considered by the CDC to be a major public health threat in the United States.[1] Patients with antibiotic resistant infections have higher morbidity and mortality, including longer hospital stays with increased costs to the healthcare system.[1] To help mitigate the consequences of antibiotic resistance, the CDC has called for improved antibiotic stewardship and the development of new diagnostic tests.[1]

Since the introduction of methicillin into clinical use, methicillin-resistant *Staphylococcus aureus* (MRSA) strains have emerged worldwide as important nosocomial pathogens with substantially increasing occurrences in the community.[2,3] MRSA is categorized as a serious threat by the CDC with more than 80,000 severe MRSA infections per year, leading to over 11,000 deaths.[1] *mecA*, a gene detected by DxWound, is an antibiotic resistance gene associated with *Staphylococcus* species, including *Staphylococcus aureus*, *Staphylococcus lugdunensis*, *Staphylococcus epidermidis* and other coagulase-negative staphylococci (CoNS).[4,5] The *mecA* gene mediates oxacillin/methicillin resistance in staphylococcal species. For example, when *mecA* is present in *Staphylococcus aureus*, then methicillin-resistant *Staphylococcus aureus* may be present.[4,5]

Indications for Ordering

The DxWound *mecA* test can be useful for any patient suspected of having a methicillin-resistant staphylococcal skin and soft tissue infection (SSTI) based on the clinician's determination of medical necessity. The DxWound test can identify *Staphylococcus aureus*, *Staphylococcus lugdunensis,* and *Staphylococcus epidermidis* directly from a wound sample without the need for culture enrichment. The presence of *mecA* may indicate resistance to oxacillin/methicillin and all ß-lactams with the exception of cephalosporins with anti-MRSA activity.[5] For example, when *S. aureus* and *mecA* are both detected, then MRSA may be present. In a patient with clinical signs and symptoms of infection, these staphylococcal and *mecA* tests may help clinicians quickly target antibiotic therapy.

Methodology

DxWound tests analyze DNA using real-time polymerase chain reaction (PCR) technology. The tests are performed on a swab sample taken directly from the site of infection without need for bacterial growth. The process is simple. First, cleanse and debride the wound as necessary. The Levine technique is then suggested for collection of the sample. The swab sample is collected in a solution that kills microorganisms at the same time as protecting microbial DNA, essentially preserving the wound microbiome in time at the point of specimen collection. DNA is detected directly from the patient specimen without culture enrichment. All DxWound tests have ≥95% accuracy and ≥99% reproducibility. Accuracy and reproducibility were established by testing reference specimens with characterized organisms or antibiotic resistance genes obtained from multiple sources including the FDA-CDC antimicrobial resistance isolate bank, commercial vendors, and other laboratories. For more information, please refer to the Technical Specifications bulletin.

Clinical Use

Staphylococcus species have an endogenous penicillin binding protein (PBP), which is vital to peptidoglycan synthesis and cell wall formation.[6-8] ß-lactams, such as methicillin or oxacillin, specifically target PBP and irreversibly inactivate the enzyme, leading to defective cell wall formation and eventually cell death.[6-8] When the *mecA* gene is active in *Staphylococcus* species, it encodes a new PBP, termed penicillin binding protein 2a (PBP2a), which results in a reduced affinity and less accessibility for ß-lactams, as well as a reduced rate of ß-lactam-mediated enzyme acylation, thus contributing to bacterial ß-lactam resistance.[6-8]

A study of samples from complicated skin and skin structure infections showed that 50.9% of *S. aureus* isolates in North America (U.S. and Canada) encoded and expressed the *mecA* gene.[9] Multiple studies have shown that MRSA is associated with longer lengths of hospital stay, and often with poorer outcomes, compared with methicillin-susceptible *S. aureus* (MSSA) or non-MRSA infections.[10,11] ß-lactam antibiotics may be used to treat infections caused by various *Staphylococcus* species. However, since *mecA* has been associated with resistance to these antibiotics, testing for this gene can help clinicians identify potential antibiotic resistant *Staphylococcus* species to rapidly target antibiotic therapy.

Coagulase-negative staphylococci are the second most common cause of surgical site infections following *S. aureus*, with *S. epidermidis* representing the most common species. *S. epidermidis* causes surgical site infections and has a propensity for biofilm formation leading to infections on valves, shunts and prostheses. Methicillin resistance is often observed (75-90% of hospital isolates) in *S. epidermidis* and resistance to other antimicrobials is also common leading to challenges in selecting appropriate antimicrobial therapy.[12, 13]

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Test Interpretation

The DxWound report provides specific information about the *mecA* gene and its association with resistance to oxacillin/methicillin and all ß-lactams with the exception of cephalosporins with anti-MRSA activity.[5] See Table 1 for additional information regarding *mecA* test interpretation.

Table 1. DxWound *mecA* Test Interpretation[14, 15]

DxWound Test Results	Potential Organism Present	Common Antibiotic Coverage	
		Oral	IV
Staphylococcal species + *mecA*	MRSA or Methicillin-Resistant Coagulase-Negative Staphylococci (MRCoNS)	Clindamycin, Doxycycline, Linezolid, Minocycline, TMP-SMX	Daptomycin, Linezolid, Vancomycin
Staphylococcal species (No *mecA*)	MSSA or Methicillin-Susceptible Coagulase-Negative Staphylococci (MSCoNS)	Cephalexin, Dicloxacillin, any MRSA active agent*	Cefazolin, Nafcillin, Oxacillin, any MRSA active agent*

* Possible alternative if patient has true penicillin allergy

Limitations

- These tests detect the presence of genes and do not detect whether the genes are expressed.
- These tests do not detect all known antibiotic resistance mechanisms, nor do they identify with which staphylococcal species *mecA* is associated.
- The use of PCR to test *S. aureus* isolates for the presence of the *mecA* gene can result in a small percentage of strains (3%) testing positive for *mecA*, but being highly susceptible to methicillin-like antibiotics.[16, 17]
- The DxWound Genetic Analysis Report does not make recommendations for treatment. All test results should be evaluated in the context of the patient's individual clinical presentation.

Technical Assistance

For technical assistance with interpretation or to speak with one of our clinical support specialists, scientists, or clinical pharmacists, please call Client Services at (877) 866-0603, Monday – Friday 5:00am to 5:00pm (Pacific Time).

Reporting

All test results are reported, generally, within 1 business day of specimen receipt. These results are available in the online portal as a DxWound Report.

How To Order

Using a CogenDx test requisition (paper or electronic), medically necessary tests are ordered by individual test based on patient-specific elements identified during the clinical assessment and documented in the patient's medical record by the provider. Submit swab specimen in the collection device provided according to the directions in the Specimen Collection Manual. A completed Documentation for DxWound Testing form is required with each order.

References

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