

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 beta-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 $\geq 95\%$ accuracy and $\geq 99\%$ reproducibility. The accuracy and reproducibility of DxWound tests were defined by either comparison to culture reports for wound samples and/or by correct identification of known organisms or antibiotic resistance genes in reference samples obtained from the FDA-CDC antimicrobial resistance isolate bank, commercial vendors, and research 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 Beta-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 beta-lactams, as well as a reduced rate of beta-lactam-mediated enzyme acylation, thus contributing to bacterial beta-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} Beta-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}

Continued on next page.

Test Interpretation

The DxWound report provides specific information about the *mecA* gene and its association with resistance to oxacillin/methicillin and all beta-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 + <i>mecA</i>	Methicillin-Resistant Staphylococcal species	Clindamycin, Doxycycline, Linezolid, Minocycline, TMP-SMX	Daptomycin, Linezolid, Vancomycin
Staphylococcal species (No <i>mecA</i>)	Methicillin-Sensitive Staphylococcal species	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.

References

- Centers for Disease Control and Prevention, Antibiotic Resistance Threats in the United States, 2013. <https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf>.
- Huletsky A, Giroux R, Rossbach V, et al. New Real-Time PCR Assay for Rapid Detection of Methicillin-Resistant *Staphylococcus aureus* Directly from Specimens Containing a Mixture of Staphylococci. *Journal of Clinical Microbiology*. 2004; 42(5): 1875-1884.
- Moet GJ, Jones RN, Biedenbach DJ, Stilwell MG, Fritsche TR. Contemporary causes of skin and soft tissue infections in North America, Latin America, and Europe: report from the SENTRY Antimicrobial Surveillance Program (1998-2004). *Diagn Microbiol Infect Dis*. 2007; 57(1): 7-13.
- Gordon RJ, Lowy FD. Pathogenesis of methicillin-resistant *Staphylococcus aureus* infection. *Clin Infect Dis*. 2008; 46 Suppl 5: S350-9.
- Patel. Performance Standards for Antimicrobial Susceptibility Testing. Clinical and Laboratory Standards Institute (CLSI) 2017; 27th ed. (CLSI supplement M100)
- Peacock SJ, Paterson GK. Mechanisms of Methicillin Resistance in *Staphylococcus aureus*. *Annual Review Biochem*. 2015; 84: 577-601.
- Deurenberg RH, Vink C, Kalenic S, Friedrich AW, Bruggeman CA, Stobberingh EE. The molecular evolution of methicillin-resistant *Staphylococcus aureus*. *Clin Microbiol Infect*. 2007; 13(3): 222-35.
- Ray GT, Suaya JA, Baxter R. Microbiology of skin and soft tissue infections in the age of community-acquired methicillin-resistant *Staphylococcus aureus*. *Diagn Microbiol Infect Dis*. 2013; 76(1): 24-30.
- Jones CH, Tuckman M, Howe AY, Orłowski M, Mullen S, Chan K, Bradford PA. Diagnostic PCR analysis of the occurrence of methicillin and tetracycline resistance genes among *Staphylococcus aureus* isolates from phase 3 clinical trials of tigecycline for complicated skin and skin structure infections. *Antimicrob Agents Chemother*. 2006; 50(2): 505-10.
- Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis*. 2003; 36(5): 592-598.
- Itani KMF, Merchant S, Lin S-J, Akhras K, Alandete JC, Hatoum HT. Outcomes and management costs in patients hospitalized for skin and skin-structure infections. *Am J Infect Control*. 2011; 39(1): 42-49.
- Otto M. *Staphylococcus epidermidis*—the 'accidental' pathogen. *Nat Rev Microbiol*. 2009; 7(8): 555-67.
- Rogers KL, Fey PD, Rupp ME. Coagulase-negative staphylococcal infections. *Infect Dis Clin North Am*. 2009 Mar; 23(1): 73-98.
- Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014; 59(2): e10-52
- Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2012; 54(12): e132-73.
- Proulx MK, Palace SG, Gandra S, et al. Reversion from Methicillin Susceptibility to Methicillin Resistance in *Staphylococcus aureus* During Treatment of Bacteremia. *J Infect Dis*. 2016; 213(6): 1041-8.
- Hososaka Y, Hanaki H, Endo H, et al. Characterization of oxacillin-susceptible *mecA*-positive *Staphylococcus aureus*: a new type of MRSA. *J Infect Chemother*. 2007; 13(2): 79-86.

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.



Contact CogenDx to learn more.
Client Services: 877.866.0603
cogendx.com