DxWound

CogenDx

Clinical Bulletin: DxWound Staphylococcus Tests

Description

Staphylococcus aureus (S. aureus) is the most common pathogen associated with skin and soft tissue infections (SSTIs).[1] DxWound identifies certain *Staphylococcal* species, along with the antibiotic resistance gene *mecA* and the virulence gene *lukF-PV* (Panton-Valentine Leukocidin virulence factor, PVL).

An antibiotic resistance gene is a gene present in bacteria that mediates resistance to a specific antibiotic or class of antibiotics. *mecA* is an antibiotic resistance gene associated with *Staphylococcus* species, including *Staphylococcus aureus, Staphylococcus lugdunensis, Staphylococcus epidermidis* and other Coagulase-Negative Staphylococci (CoNS). The *mecA* gene mediates oxacillin/methicillin resistance. When *mecA* is present in *Staphylococcus aureus*, then Methicillin-resistant *Staphylococcus aureus* (MRSA) may be present.

Panton-Valentine Leukocidin (PVL) is a virulence factor encoded by two genes: *lukS-PV* and *lukF-PV*. The presence of PVL in *S. aureus* appears to be associated with increased infection severity, with PVL-positive infections being more likely to lead to necrosis and more likely to require surgery.[2-4]

Indications for Ordering

The DxWound *Staphylococcal tests* can be useful for any patient suspected of having a *Staphylococcal* skin and soft tissue infection (SSTI) based on the clinician's determination of medical necessity. The DxWound tests can identify *S. aureus* 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] When *S. aureus* and mecA are both detected, then MRSA may be present. The presence of PVL may suggest increased infection severity.[2-4] In a patient with clinical signs and symptoms of infection, these *Staphylococcal* tests may help clinicians quickly target antibiotic therapy.

Methodology

DxWound is a polymerase chain reaction (PCR)-based assay which analyzes microbial DNA using species-specific DNA sequences, such as 16S rRNA sequences for bacterial detection. In addition, sequences specific to virulence gene and mecA genes are also analyzed.

DxWound utilizes a swab for sample collection. The tests are performed on a sample taken directly from the wound. The swab sample is collected in an inactivating solution that kills the microorganisms at the same time as protecting the microbial DNA, thus preserving the wound microbiome in time at the point of specimen collection. (For more information, see Technical Specifications bulletin). DNA is detected directly from the patient specimen without culture enrichment.

Clinical Use

S. aureus is the most common pathogen associated with SSTIs[1], with MRSA becoming increasingly common in both the inpatient setting (hospital acquired infections) and the outpatient (community) setting.[6] In one study, almost 80% of positive SSTI cultures detected *S. aureus*, and about 50% of those were MRSA.[7] MRSA has been tied to increased hospital lengths of stay, increased healthcare costs, is an independent risk factor for mortality[8,9] and is now predictably resistant to all ß–lactam antibiotics except ceftaroline.[5] As such, MRSA is considered a serious threat by the CDC.10 According to Amin et al.,[6] "the increasing incidence of SSTIs in both ambulatory and hospital settings, coupled with the increase of MRSA as a causative pathogen, demands optimal management of these infections to improve outcomes."

S. aureus can also express virulence factors that are associated with increased infection severity.[2] The presence of the PVL virulence factor in *S. aureus* is associated with infections that are more likely to lead to necrosis and more likely to require surgical treatment.[2-4]

The failure of empiric therapy is a concern in treatment of SSTIs. One study suggested that as many as 16.6% of acute SSTIs, 34.1% of chronic or ulcerative infections, and 26.7% of surgical site infections had initial treatment failure. It has been shown that antimicrobial therapy which is not targeted to the causative pathogen within 48-hours of presentation is an independent risk factor for treatment failure.[11,12]

Clinicians can use the DxWound *Staphylococcal* results to help them quickly target antibiotic therapy, ideally within that important 48-hour window.

Continued on next page.

Test Interpretation

These tests identify if *Staphylococcus* spp, the *mecA* gene or PVL gene are present. The DxWound report provides specific information about the *mecA* gene and its association to resistance to oxacillin/methicillin and all ß–lactams with the exception of cephalosporins with anti-MRSA activity. If both *S. aureus* and *mecA* are positive, then MRSA may be present. The DxWound report also indicates that if PVL is detected, there may be increased infection severity and the potential need for surgical intervention. Clinically, these test results may help clinicians quickly target antibiotic therapy. It is important to note that these tests do not detect all known antibiotic resistance mechanisms or virulence factors, nor do they definitively identify which organism is associated with an antibiotic resistance gene.

Limitations

- These tests detect the presence of genes and does not detect whether the genes are expressed.
- These tests do not detect all known antibiotic resistance mechanisms, nor does identify with which Staphylococcal species *mecA* is associated.
- It is possible that *mecA* is associated with an organism that is not included in the test.
- In addition to *Staphylococcus aureus* and *Staphylococcus lugdunensis*, *mecA* can also be associated with *S. epidermidis*, a CoNS which is commonly found in normal skin flora and is not detected by DxWound.[13] More than 70% of opportunistic *S. epidermidis* are resistant to oxacillin/methicillin.[14,15]
- 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 VIRA online portal as a DxWound Report.

How To Order

Using the VIRA online portal, 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 of Medical Necessity Form is required with each order.

References

1. 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
2. Watkins RR, David MZ, Salata RA. Current concepts on the virulence mechanisms of meticillin-resistant Staphylococcus aureus. *J Med Microbiol* 2012;61:1179-93
3. Shallcross LJ, Fragaszy E, Johnson AM, Hayward AC. The role of the Panton-Valentine leucocidin toxin in staphylococcal disease: a systematic review and meta-analysis. *Lancet Infect Dis* 2013;13(1):43-54
4. Gordon RJ, Lowy FD. Pathogenesis of methicillin-resistant Staphylococcus aureus infection. *Clin Infect Dis* 2008;46 Suppl 5:S350-9
5. Patel. Performance Standards for Antimicrobial Susceptibility Testing. Clinical and Laboratory Standards Institute (CLSI) 2017;27th ed.(CLSI supplement M100)
6. Amin AN, Cerceo EA, Deitelzweig SB, Pile JC, Rosenberg DJ, Sherman BM. Hospitalist perspective on the treatment of skin and soft tissue infections. *Mayo Clin Proc* 2014;89(10):1436-51
7. 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
8. 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.
9. 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.
10. U.S. Department of Health and Human Services Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. https://www.cdc.gov/drugresistance/threat-report-2013/. Accessed April 18, 2017.
11. Berger A, Oster G, Edelsberg J, Huang X, Weber DJ. Initial treatment failure in patients with complicated skin and skin structure infections. *Surg Infect*. 2013;14(3):304-312.
12. Ruhe JJ, Smith N, Bradsher RW, Menon A. Community-onset methicillin-resistant Staphylococcus aureus skin and soft-tissue infections: impact of antimicrobial therapy on outcome. *Clin Infect Dis*. 2007;44(6):777-784.
13. Otto M. Staphylococcus epidermidis–the 'accidental' pathogen. *Nat Rev Microbiol*. 2009;7(8):555-67
14. Wisplinghoff H, Rosato AE, Enright MC, Noto M, Craig W, Archer GL. Related clones containing SCCmec type IV predominate among clinically significant Staphylococcus epidermidis isolates. *Antimicrob Agents Chemother* 2003;47(11):3574-9
15. Hanssen AM, Ericson Sollid JU. SCCmec in staphylococci: genes on the move. *FEMS Immunol Med Microbiol* 2006;46(1):8-20
16. 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
17. 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

CogenDx

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

CogenDx is a brand of Millennium Health, LLC. The CogenDx logo is a service mark or registered service mark of Millennium Health, LLC or its subsidiaries in the United States and other countries. All other trademarks used herein are the property of their respective owners.

DXW-015-V01 © 2017 Millennium Health, LLC 08/2017