



LGM NEWS

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Laboratory Detection of Borderline-Oxacillin Resistant *Staphylococcus aureus* (BORSA)

By: Eric Ransom, PhD, and Carey-Ann Burnham, PhD

Staphylococcus aureus is a Gram-positive bacterium that can be a skin commensal or a potent pathogen. A key factor in evaluating antimicrobial treatment options is determining if the isolate is deemed methicillin-resistant *S. aureus* (MRSA, conferred by *mecA*) or methicillin-susceptible *S. aureus* (MSSA). MRSA isolates are resistant to beta-lactam antibiotics such as cefazolin, oxacillin, and ceftriaxone. Clinical microbiology laboratories have several methods at their disposal to determine if an isolate is MSSA or MRSA. Most of these methods are designed to detect the most prevalent MRSA resistance mechanism: penicillin binding protein modification (PBP2a) encoded by the *mecA* gene.

Borderline-Oxacillin Resistant *Staphylococcus aureus* (BORSA) is another category of resistant *S. aureus*. The underlying resistance mechanism of BORSA is not entirely understood, but hyperproduction of β -lactamase enzymes is thought to be an important factor in the resistance profile of these strains. Prevalence rates of BORSA varies in the literature but is considered to be relatively rare (<5% of all methicillin-susceptible *S. aureus* isolates in most healthcare settings). Because of this low prevalence and uncertainty of the specific resistance mechanism, testing for BORSA is challenging and is not usually performed. This has resulted in BORSA isolates routinely being misclassified as oxacillin susceptible. As far as treatment for BORSA infections, the literature is limited and variable (for more information see “Borderline oxacillin-resistant *Staphylococcus aureus* (BORSA) – a more common problem than expected?” a review by Hryniewicz and Garbacz in *J. Med Micro* 2017;66:1367–1373). *continued on page 2*



Laboratory Detection of Borderline-Oxacillin Resistant *Staphylococcus aureus* (BORSA) continued from page 1

By: Eric Ransom, PhD, and Carey-Ann Burnham, PhD

BORSA became of great interest locally when an investigation, in collaboration with St. Louis Children's Infection Prevention, found a higher than expected prevalence of BORSA in the neonatal ICU. While this investigation concluded there was no outbreak, the findings highlighted the importance of accurately identifying BORSA strains. The BJH microbiology laboratory has implemented new processes to better identify BORSA in December of 2020. While we expect this phenotype to be rare, it would manifest as *mecA* negative, oxacillin-intermediate or -resistant strains, and a comment would be added to the report to reflect this phenotype.

If you have questions about these testing changes, please contact the microbiology laboratory at 314-362-3898 or Carey-Ann Burnham, PhD, Medical Director of Clinical Microbiology, at cburnham@wustl.edu.

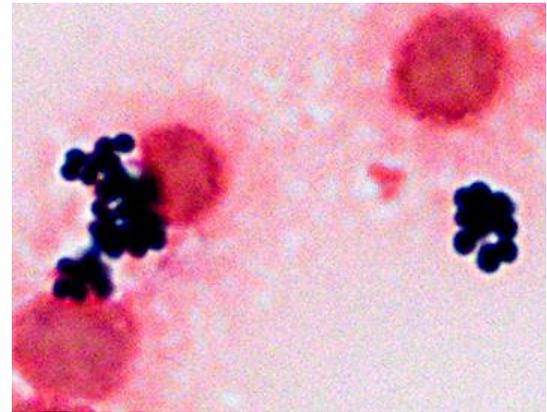


Figure 1: The Gram-positive cocci in clusters of *S. aureus* from a blood culture.

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Update on Specimen Collection for Upper Respiratory Pathogen Testing

By: Melanie Yarbrough, PhD

The BJH microbiology laboratory offers a variety of molecular testing options for detection of upper respiratory tract pathogens, including influenza and SARS-CoV-2. With so many testing options, collection of the correct specimen type is critical to ensure appropriate testing and maximize analytical sensitivity. Comprehensive testing is available for patients with respiratory symptoms, while dedicated SARS-CoV-2 testing is available for patients without symptoms.

Testing on Symptomatic Patients		
Available Testing	Influenza/RSV PCR	
	Influenza/RSV/COVID-19 PCR	
	Respiratory Pathogen Panel (aka RPP, RVP, Biofire)	
Body Site	Nasopharyngeal (NP) swab	
Collection Device	Flexible minitip swab with 3 mL of Universal Transport Media/UTM (Red cap tube)	

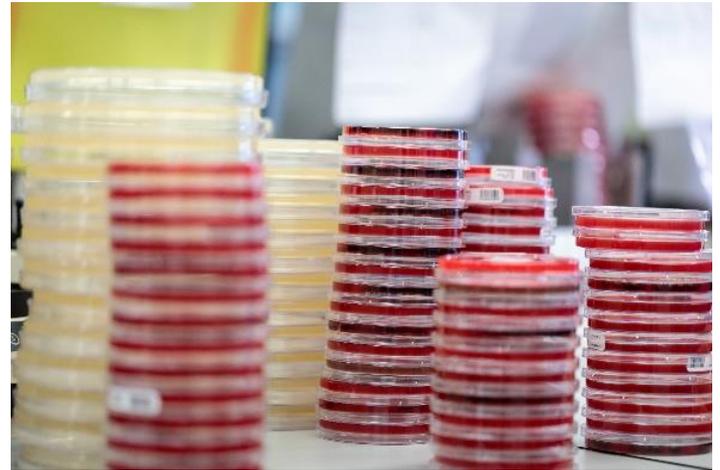
Testing on Asymptomatic Patients				
Available Testing:	COVID-19 PCR		COVID-19 antigen	
Collection devices appropriate for indicated body site:				
Oropharyngeal (OP) swab		Nasopharyngeal (NP) swab		
Flexible minitip swab with Universal Transport Media/UTM (Red cap)	ESwab Transport System (Regular flocced swab)	Flexible Minitip ESwab (Blue cap)	Minitip ESwab (Green cap)	Flexible minitip swab with Universal Transport Media/UTM (Red cap)



Evaluation of the activity of the novel antibiotic Cefidericol for testing against resistant *Enterobacterales* and *Pseudomonas aeruginosa*

By: Robert Potter, PhD and Carey-Ann Burnham, PhD

Cefidericol is a novel cephalosporin-siderophore antibiotic for the treatment of multidrug resistant Gram-negative bacteria such as carbapenem-resistant *Enterobacterales* and *Pseudomonas aeruginosa*. Similar to other cephalosporin antibiotics, the lethal mechanism of action is due to inhibition of penicillin binding proteins leading to lysis of the bacteria. Siderophores are metal chelating molecules produced by bacteria to scavenge iron and other essential metals from the environment. The siderophore portion of cefidericol is able to bind iron, after which it is actively transported into the periplasmic space by Gram-negative bacteria, where it is able to inhibit penicillin binding proteins.



Cefidericol shows a wide spectrum of activity against Gram-negative bacteria and in the 30th edition of the Clinical & Laboratory Standards Institute M100 document has breakpoints for *Enterobacterales*, *P. aeruginosa*, *Stenotrophomonas maltophilia*, and *Acinetobacter baumannii*. We have recently validated Cefidericol Kirby-Bauer disk diffusion against retrospectively collected multidrug resistant *Enterobacterales* (5 *Enterobacter cloacae*, 8 *Escherichia coli*, 12 *Klebsiella pneumoniae*) and *Pseudomonas aeruginosa* (n=23). We found that 2 of the 25 *Enterobacterales* were non-susceptible, including a *bla*_{NDM}-harboring *E. coli*. For *P. aeruginosa*, 2 of 23 isolates were resistant to cefidericol, both were negative for known carbapenemases but had a mucoid phenotype. Mechanisms of resistance to cefidericol are not well understood but is thought to be connected to iron uptake porin expression. Susceptibility testing is important in cases where this antimicrobial agent will be used for treatment.

Clinical testing for Cefidericol for *Enterobacterales* and *P. aeruginosa* will be available in the BJH Microbiology Laboratory in 2021. For additional information, please contact Carey-Ann Burnham, PhD, Medical Director of Clinical Microbiology at cburnham@wustl.edu.

DID YOU KNOW?

So far, BJH has distributed over 250 units of COVID convalescent plasma for transfusion!



SARS-CoV-2: One Virus, Many Tests

By: Bijal Parikh, MD, PhD

Within a short span of time, the regulatory and diagnostic landscape for SARS-CoV-2 testing has shifted rapidly: FDA oversight through Emergency Use Authorizations (EUA) are no longer needed for laboratory developed tests, multiple analytes have been shown to be comparable for diagnostic and screening purposes, and a plethora of specimen types and collection devices have been validated for clinical use.

The major milestones in our diagnostic journey are highlighted below (see figure). This graphic also summarizes how our capacity has grown as we constantly battle supply chain shortages in every aspect of (SARS-CoV-2 and non-SARS-CoV-2) testing, including media, swabs, pipet tips, extraction reagents, extractors, PCR machines, and sample-to-answer testing platforms.

This complexity often leads to several questions surrounding our SARS-CoV-2 test options, including:

- Why does the lab need so many different testing platforms?
- Are they equally sensitive?
- How does the lab decide which sample is performed on a particular platform?

The laboratory needs to maintain multiple test platforms to anticipate changes in the tenuous supply chain, sustain the ability to test diverse specimen types, provide redundancy if one method is unavailable for an extended time, and maintain turnaround times.

While all methods vary in terms of absolute sensitivity, SARS-CoV-2 diagnostics are qualitative tests and as such, all of the assays are validated consistent with CAP/CLIA regulatory requirements with the majority also authorized by the FDA. The clinical performance of all of the PCR-based tests in use at our medical center is equivalent.

The different SARS-CoV-2 PCR platforms differ not so much in accuracy but more in complexity and turnaround times. Therefore, the routing of specimens to particular platforms is a decision led by hospital and university leadership who consider multiple factors including test capacity, test populations, clinical urgency, and evolving public health recommendations. Moreover, supply shortages for COVID-19 testing have necessitated our laboratory to implement pooled diagnostic testing.

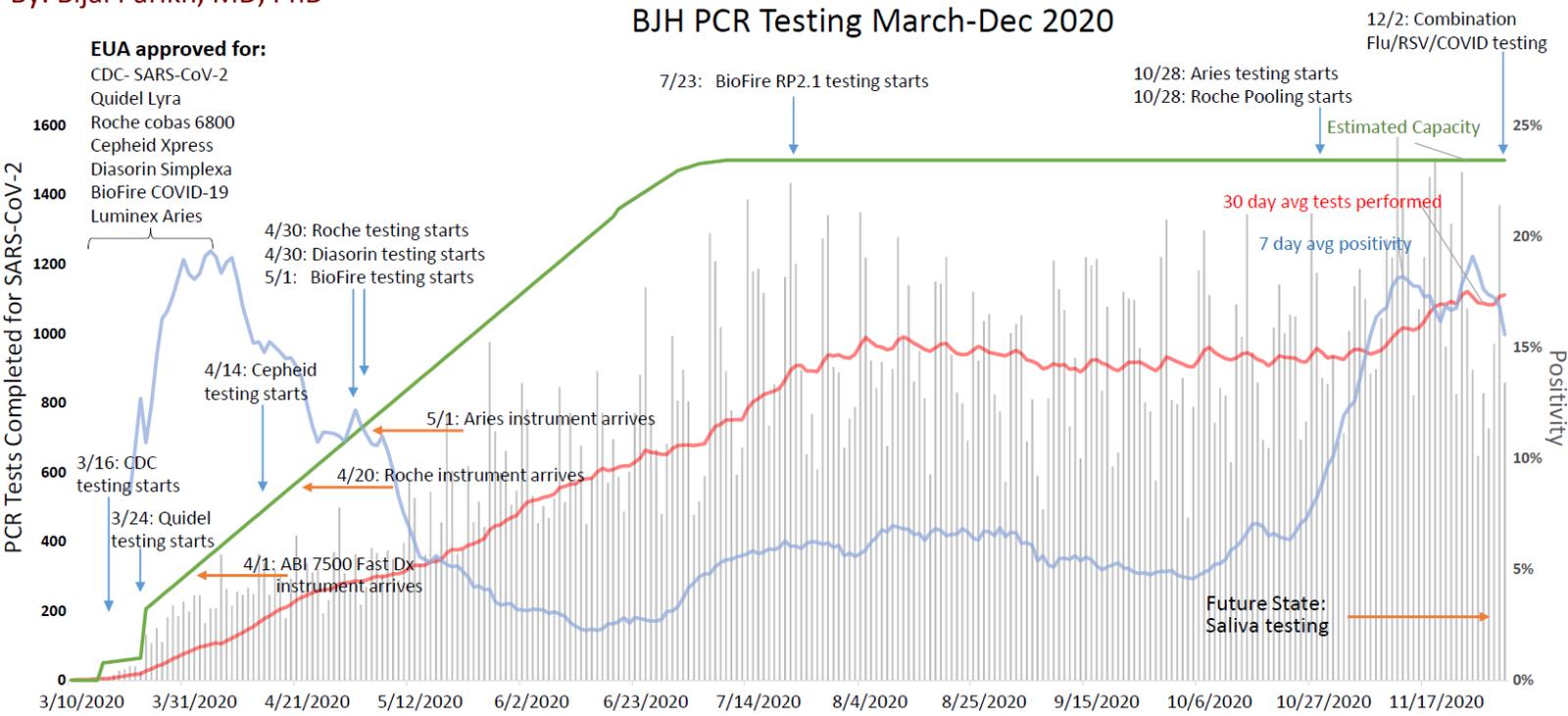
While we have been testing for SARS-CoV-2 for less than a year, the COVID-19 volume now accounts for >80% of all specimens routed through the BJH Molecular Infectious Disease (MID) Laboratory! Total testing volume in the MID Laboratory has dramatically expanded from 5,000 per month pre-COVID to 35,000 per month currently. However, testing volumes will continue to change. Widespread COVID-19 vaccination is some time away, flu season is nearly here. Therefore, we remain focused on ensuring diagnostic accuracy, decreasing turnaround times, expanding testing availability, and maintaining reliable high-quality testing options. *continued on page 6*



SARS-CoV-2: One Virus, Many Tests *continued from page 5*

By: Bijal Parikh, MD, PhD

BJH PCR Testing March-Dec 2020



LGM Featured Colleague



Dr. Yang Cao joined the LGM faculty in July 2017 as Assistant Professor and Associate Medical Director of Clinical Cytogenomics and Molecular Pathology Laboratory. She received her Ph.D. in genetics from the University of Wisconsin-Madison, where she focused on investigating genetic and molecular mechanisms of neurodegenerative disorders using forward genetics strategy. She completed her fellowship training in Clinical Cytogenomics and Clinical Molecular Genetics at Mayo Clinic, and became a dual board-certified laboratory geneticist.

In LGM, Dr. Cao has clinical and teaching responsibilities in the Clinical Cytogenomics and Molecular Pathology Laboratory, on the Clinical and Translational Genomics next generation sequencing (NGS) service and the BJC Molecular Diagnostic Laboratory short tandem repeat analysis service. Dr. Cao's scope of practice includes clinical service, assay development and validation, laboratory quality assurance/quality control and trainee education. She also teaches clinical cytogenomics lectures in undergraduate and graduate level courses at Wash U.

Dr. Cao's clinical research interests focus on the identification of clinical significance of copy number variants and somatic variants in constitutional diseases, especially in neurodevelopmental disorders and brain malformation. She has been actively involving in national professional communities, such as Clinical & Laboratory Standards Institute document development committee, ClinGen Gene Dosage Sensitivity Working Group and Brain Malformation Pooling Expert Panel. Dr. Cao would like to devote her efforts to improving clinical service and educational environment of clinical genomics, which she believes is truly an essential component of precision medicine.