Background. Waiting for culture availability from orthopedic hardware (HW) infections delays patient discharge and time to definitive antimicrobial therapy. In February 2017, Vanderbilt University Hospital (VUH) implemented a penicillin-bind- ing protein 2a-based rapid diagnostic, Alere, to differentiate methicillin-resistant S. aureus (MSSA) and methicillin-resistant S. aureus (MRSA) from tissue sample growth. In other settings, use of Alere demonstrated decreased time to definitive therapy with and without stewardship intervention. However, no studies to date have examined the impact of Alere in the orthopedic HW infection population.

Methods. We performed a retrospective study of patients ≥18 years of age admitted to VUH with a culture-positive, monomicrobial, S. aureus orthopedic HW infection. Select ICO-10 codes related to orthopedic HW infections were used to identify potential patients. Exclusion criteria included concomitant bacteremia or polymicrobial infections. Patients with sterile site cultures obtained from August 2016 to January 2017 were included in the pre-Alere group and February 2017 to September 2017 in the post-Alere group. The primary outcome was to provide appropriate antibiotic, defined as cefoxitin or nafcillin for MSSA, and vancomycin for MRSA. Daptomycin and linezolid were acceptable alternatives in the case of prior vancomycin failure, or severe toxicity of vancomycin.

Results. ICO-10 codes identified a total of 331 patients, with 29 (8.7%) demonstrating monomicrobial S. aureus HW infections (52% MSSA). There were 11 (38%) and 18 (62%) patients in pre- and post-Alere groups, respectively. Alere results provided definitive results for FOS in 31/9 (34.5%) and 41.8 hours less in post-Aler group (P = 0.009). Duration of empiric Gram-negative coverage was significantly reduced in the post-Alere group (P = 0.029). Overall length of stay was unchanged between the groups (P = 0.873).

Conclusion. Introduction of Alere reduced time to appropriate antibiotic and reduced empiric Gram negative coverage in patients being treated for orthopedic hardware infections.

Disclosures. All authors: No reported disclosures.

2062. Evaluation of Susceptibility Testing Methods for Fosfomycin Against Enterobacteriaceae and Pseudomonas aeruginosa

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Background. Fosfomycin (FOS) is a broad-spectrum bacterial agent that has been suggested as an alternative treatment option for infections caused by multi-drug resistant Gram-negatives. The approved in vitro antimicrobial susceptibility testing method for FOS is agar dilution (AD) and disk diffusion (DD); however, broth microdilution (BMD) is the basis of automated systems used in clinical microbiology laboratories. Herein we evaluated the accuracy of BMD and DD vs. the gold standard AD for FOS susceptibility tests.

Methods. S. aureus (39 E. coli), 33 K. pneumoniae (Kp), 9 Enterobacter spp., (Ent); and 59 P. aeruginosa (Pae), were determined by BMD, DD and AD. Mueller–Hinton supplemented with 25 mg/L glucose 6-phosphate (G6P) was used for BMD and AD; results were interpreted according to CLSI and EUCAST guidelines. For DD screening, 50 μg FOS discs supplemented with 50 μg G6P were used and interpretation was performed following the Fos. For Pae, the EUCAST epidemiological cutoff was used. Concordance of BMD and DD with AD is reported in terms of categorical agreement (CA), as defined as results between the two methods that matched based on the interpretative breakpoint proposed; false-resistant results to be major errors (ME); and false-susceptible results to be very major errors (VME).

Results. According to AD, the susceptibility to FOS of Eco, Kpn, Ent, and Pae was 97.4, 72.7, 100, and 98.3% respectively. Concordance analysis between BMD and DD with the gold standard AD is shown in Table 1.

Conclusion. The high proportion of ME found with BMD, which is used in the automated systems may cause an overestimation of the FOS resistance, especially in Kpn and Ent. Thus, we suggest that microbiology laboratories confirm resistant strains by BMD. DD may be useful for Eco and Ent, when scattered colonies within inhibition zones are observed. Thus, we suggest that microbiology laboratories confirm resistant strains by BMD.

Disclosures. C. Hernandez, MSD: Consultant, Consulting fee and Speaker honorarium; Pfizer: Consultant, Consulting fee and Speaker honorarium. C. Palleares, Pfizer: Consultant, Consulting fee and Speaker honorarium. M. V. Villegas, MSD: Grant Investigator, Grant recipient and Speaker honorarium; Pfizer: Grant Investigator, Grant recipient and Speaker honorarium; Zambon: Grant Investigator, Grant recipient. W. Miller: Consultant, Consulting fee and Speaker honorarium. M. A. Grant Investigator, Grant recipient.

2063. Extracellular Release of β-Lactamase Is Responsible for the Cefazolin Inoculum Effect (CzIE) inmethicillin-Susceptible Staphylococcus aureus

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Background. Cefazolin is becoming first-line therapy for MSSA infections since it appears to be better tolerated than oxazolidinones with similar outcomes. An inoculum effect when using cephalosporins as first-line therapy for MSSA is the CzIE, defined as MICs ≥ 16 mg/L when performed at high bacterial inoculum (107 CFU/ml) compared with standard inoculum (105 CFU/ml). We postulated that release of BlaZ (a lipoprotein) to the extracellular milieu is the mechanism responsible for the CzIE. Confirmation of this phenomenon would permit developing a rapid test to identify this phenomenon in clinical settings.

Methods. We monitored the hydrolysis of 50 μM of nitrocefin by S. aureus supernatants after incubation with ampicillin (150 μg/mL) for 1 h. A total of 150 μL of supernatants was used to inoculate nitrocefin at 25°C in 20 mM HEPES, pH 7.4, 100 mM NaCl for 30 minutes. Nitrocefin hydrolysis was monitored by following the change in absorbance at 482 resulting from opening of the β-lactam ring of nitrocefin. Visual inspection to monitor color changes was also performed. We identified 3 strains of MSSA (S. aureus TX0117, a well-characterized strain that exhibits the CzIE; (ii) TX0117c, a derivative of TX0117 that harbors a mutation inactivating BlaZ and abolishing the CzIE, and (iii) ATCC 29213 a BlaZ-positive strain that lacks the CzIE. Subsequently, we validated the methodology in 10 South American isolates of different backgrounds that had been previously characterized for the CzIE.

Results. A statistically significant difference in ODs after 30 minutes was observed in TX0117 (CzIE) vs. TX0117c (no CzIE) and ATCC 29213 (no CzIE) (all P < 0.001), suggesting high BlaZ activity in supernatants of TX0117 and supporting the release of the enzyme as the main mechanism of the CzIE. All South American isolates that exhibited the CzIE; (ii) TX0117c, a derivative of TX0117 that harbors a mutation inactivating BlaZ and abolishing the CzIE, and (iii) ATCC 29213 a BlaZ-positive strain that lacks the CzIE. Subsequently, we validated the methodology in 10 South American isolates of different backgrounds that had been previously characterized for the CzIE.

Conclusion. The CzIE is likely due to release of BlaZ to the extracellular milieu. A rapid test that can readily identify MSSA strains exhibiting the CzIE is feasible.

Disclosures. W. Miller, Mercier: Investigator, Research support. C. Arias, Merck & Co., Inc.: Grant Investigator, Research support; MEd: Grant Investigator, Research support; Allergan: Grant Investigator, Research support.

2064. Rapid Detection of Carbenapenem-Producing Klebsiella pneumoniae (CPK) Directly by Respiratory Secretion and Clinical Characteristics of Patients with CPK from a 1,200 Bed Tertiary Care Hospital in Thailand

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Background. There is an unmet need for rapid detection of carbenapenem-producing Klebsiella pneumoniae (CPK) for patient care and infection control. The BD MAX™ CRE (automated PCR, Geneohm, Canada) test is the fully automated sample-to-result platform for detection of resistance genes, blaOXA-48, blaVIM, and blalCM within 2 hours. It has been validated for use with colonies and rectal swab. We aimed to evaluate its performance for detection of carbenapenemases directly from respiratory samples of the patients whom K. pneumoniae (KP) were identified.

Methods. A total of 169 KP isolates and respiratory samples were collected from patients admitted to King Chulalongkorn Memorial Hospital, Bangkok, Thailand from...
June 2017 to December 2017. The automated PCR test was performed directly from respiratory specimens. The results were compared with in-house PCR for detection of carbapenemase genes performed on KP colonies isolated from respiratory specimens as our reference method. Patient and clinical characteristics between patients with CPK and non-CPK were also analyzed.

Results. The prevalence of CPK was 10.6% (18/169 isolates). The automated PCR test had 91.12% accuracy, 66.7% sensitivity (95% CI, 49.9–83.8%), 94.0% specificity (95% CI, 88.9–96.3%), 57.1% positive predictive value (95% CI, 39.5–73.2) and 95.9% negative predictive value (95% CI, 92.4–97.85). Of 18 isolates, bla\textit{carb} was the most common carbapenemase gene (17 isolates; 94.4%), followed by bla\textit{OXA-48} (7 isolates; 38.9%). A combination of bla\textit{carb} and bla\textit{OXA-48} was detected in 6 isolates (33.3%). There were 7 (38.8%) colonizations and 11 (61.1%) infections. The significant risk factors for CPK included post-surgery (P = 0.04) and prior antibiotics exposure (P = 0.04). There was a trend toward higher mortality in patients with CPK albeit not significantly (33% vs. 24.5%, P = 0.41).

Conclusion. The automated PCR test has an acceptable accuracy with fair sensitivity for the detection of carbapenemase genes. It is unique that OXA-48 and OXA-48/NDM-1 gene combination is found in the same isolates in our institute. This diagnostic test may be used for rapid diagnosis or infection control purposes. Exposure to antibiotics associated with colonization or infection with CPK. Patients with CPK had higher mortality.

Disclosures. All authors: No reported disclosures.

2065. Whole Genome Sequencing for Antimicrobial Resistance Prediction in MRSA and VRE: A Real-world Application

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Session: 232. Diagnostics: Resistance Testing

Saturday, October 6, 2018: 12:30 PM

Background. The antimicrobial resistance (AMR) crisis represents a serious threat to public health and the healthcare economy. The impact of increasing AMR has resulted in concentrated efforts to increased rapid molecular diagnostics of AMRs. In combination with publicly available web-based AMR databases, whole-genome sequencing (WGS) offers the capacity for detection of antibiotic resistance genes with low turnaround times and is becoming increasingly affordable. Here we sought to examine concordance between WGS-based resistance prediction and phenotypic susceptibility testing results for prospectively collected VRE and MRSA clinical isolates using publicly available tools.

Methods. MRSA and VRE isolates were prospectively collected and underwent WGS at the University of Pittsburgh Medical Center (UPMC) between December 2016 and December 2017. Antibiotic-resistant gene content was assessed by uploading assembled contigs to ResFinder, NCBI betalactamase and CARD using a BLASTn search. Routine susceptibility was performed by Microscan®. Concordance between genotypic and phenotypic as well as sensitivity, specificity, positive and negative predictive values methods were calculated for each antibiotic/organism combination, using the phenotypic results as the gold standard. In case of discordance between the methods, repeat susceptibility using disc diffusion results was performed and was then considered to be the gold standard method.

Results. Phenotypic susceptibility testing and WGS results were available for 109 and 105 unique MRSA and VRE isolates, respectively. Out of total of 1,058 isolate/antibiotic combinations overall concordance of WGS-vs.-based prediction with phenotypic susceptibility methods was 99.1% with a sensitivity, specificity, PV and NPV of 99.6, 99.5, and 98.3%, respectively. Specific concordance for MRSA isolates was 98.8%, with a sensitivity, specificity, PV and NPV of 97.6, 99.8, 99.7, and 98.5% (Table 1), while concordance for VRE isolates was 99.3%, with a sensitivity, specificity, PV and NPV of 98.6, 98.1, 99.1, and 97.2% (Table 2).

Conclusion. WGS is a reliable predictor of phenotypic resistance for both MRSA and VRE.

Table 1: MRSA WGS and phenotypic resistance concordance

| Antibiotic | Total Number of isolates with both WGS and susceptibility methods | Resistance by WGS | Resistance by phenotypic susceptibility methods | Concordance with differences (%) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|------------|---------------------------------------------------------------|-------------------|--------------------------------------------|-------------------------------|----------------|---------------|---------|---------|
| Meropenem  | 109 (100.0)                                                  | 100 (100)        | 100 (100)                                  | 100 (100)                    | 100            | 100           | 100     | 100     |
| Erythromycin| 102 (94.4)                                                   | 98 (95.1)        | 99 (96.1)                                  | 100 (100)                    | 98.1           | 96.3          | 95.3    | 97.2    |
| Ceftazidime| 104 (95.3)                                                   | 98 (94.2)        | 99 (96.1)                                  | 100 (100)                    | 95.1           | 95.3          | 95.3    | 97.2    |
| Ceftiraxone| 103 (95.1)                                                   | 98 (95.1)        | 99 (96.1)                                  | 100 (100)                    | 95.1           | 95.3          | 95.3    | 97.2    |
| Gentamicin | 101 (93.5)                                                   | 98 (97.0)        | 99 (96.1)                                  | 100 (100)                    | 95.1           | 95.3          | 95.3    | 97.2    |
| Vancomycin | 100 (97.0)                                                   | 100 (100)        | 100 (100)                                  | 100 (100)                    | 100            | 100           | 100     | 100     |

*With the additional step of confirming for positive results in household genic screens, specificity, sensitivity, NPV and PPV was 100%.

2066. Accelerated Detection of Carbapenem Resistance Mechanisms in Enterobacteriaceae by MALDI-TOF Mass Spectrometry using the Direct-on-Target Microdroplet Growth Assay (DOT-MGA)

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Session: 232. Diagnostics: Resistance Testing

Saturday, October 6, 2018: 12:30 PM

Background. The differential identification of carbapenemases relays mostly on molecular techniques. Current phenotypic methods require 18 hours of incubation. We propose a matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) based direct-on-target microdroplet growth assay (DOT-MGA) aiming to offer an easy and rapid phenotypic identification of AmpC, KPC, MBL and OXA production.

Methods. Seven well-characterized Enterobacteriaceae strains recommended by EUCAST for carbapenemase detection were analyzed. Synergy between carbapenem and carbapenemase inhibitors (phenylboronic acid, aminophenylboronic acid, clavulanate, dipicolinic acid, ethylenediaminetetraacetic acid, and avibactam) and temocillin resistance were determined using a testing panel developed on a 96-spot MALDI-TOF MS target (MBT Biotarget 96, Bruker Daltonics, Germany). Microdroplets (6 µl) containing bacterial suspension and antibiotic or antibiotic/inhibitor in cation-adjusted Mueller–Hinton broth were spotted on the target and incubated for 4 hours at 36°C in a humidity chamber to avoid evaporation. The medium was subsequently removed and MALDI-TOF IMS of the cells adhering to the target were performed. The minimum inhibitory concentration (MIC) was considered to be the lowest concentration at which the MALDI Biotyper software yielded no organism identification. Synergy was defined by an eightfold or greater reduction of the meropenem MIC in the presence of an inhibitor. The absence of synergy between meropenem and inhibitors as well as high-level temocillin resistance was considered suggestive of OXA production. Results were processed and interpreted with a computer-based algorithm.

Results. After 4 hours, the method was able to correctly detect the foreknown resistance mechanisms of all tested strains (KPC, MBL, OXA, and AmpC), yielding results that agreed with those obtained by performing broth microdilution with 18 hours of incubation.

Conclusion. The DOT-MGA approach allowed easy identification and differentiation of carbapenemase production, delivering reliable results one day earlier than the usual phenotypic methods, thus displaying great potential for the clinical setting.

Disclosures. E. A. Idelevich, Bruker Daltonik: Co-inventor of a pending patent, Licensing agreement or royalty and Speaker honorarium. K. Sparbier, Bruker Daltonik: Employee, Salary. M. Kostrewza, Bruker Daltonik: Employee, Salary. K. Becker, Bruker Daltonik: Co-inventor of a pending patent, Licensing agreement or royalty and Speaker honorarium.

2067. Novel Methodology for Same-Day Antimicrobial Susceptibility Testing on VITEK 2 for Gram-Negative Rod Bacteremia

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Session: 232. Diagnostics: Resistance Testing

Saturday, October 6, 2018: 12:30 PM

Background. bloodstream infections with Gram-negative rods are potentially fatal, and specific tailored antimicrobial treatment. Optimizing therapy is currently limited by the 1-2 days turnaround time required for antimicrobial susceptibility testing. Novel same-day technologies have been developed but are expensive. Here, we describe and investigate the accuracy of a repurposed existing technology (VITEK 2, bioMérieux) for same-day susceptibility testing directly from positive blood cultures.

Methods. Starting in August 2017, patients with blood cultures positive for Gram-negative rods were prospectively included. In addition, aerobic and anaerobic blood culture bottles were spiked with a standardized inoculum of enteric Gram-negative rods from a repository of frozen samples. Positive blood cultures were processed using...