641. Evaluation of the FilmArray Pneumonia Panel and Potential Impact of Antimicrobial Use on Patients in a Trauma and Medical Intensive Care Unit
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Thursday, October 3, 2019: 12:15 PM
Background. Organisms causing infections of the lower respiratory tract in hospitalized patients can lead to high morbidity and mortality. Identification of the agents of pneumonia allows implementation of appropriate antimicrobial therapy and fast and accurate results are essential for the application of the correct antimicrobial regimen.
Methods. For 6 months results of quantitative bronchoalveolar lavage (Q-BALs) respiratory cultures, ordered as a standard of care for patients in our intensive care unit, were compared with the results obtained by a new multiplex molecular assay for the detection of lower respiratory tract pathogens, the FilmArray pneumonia panel (PP). The panel offers semi-quantitation of the bacterial targets that were compared with the quantitative results of the Q-BALs. Additionally, a retrospective chart review was performed to examine whether there would be any difference in the timing of appropriate antimicrobial therapy if the results of the panel were to be available for those patients. Appropriate antimicrobial therapy was determined according to the institutional protocol for treatment of patients for ventilator-associated pneumonia based on the results of the quantitative cultures.
Results. Thirty-six unique patients Q-BALs were run and of those there was 82% agreement on the detected targets between cultures and PP. Six targets were not detected by the panel (yeast, S. maltophilia, Streptococci, Salmonella spp.). M. catarrhalis, S. agalactiae and 3 viral targets were detected only by the panel. There was 100% agreement between the panel detected resistance markers and the culture isolates susceptibilities. Of the 36 patients, 12 were excluded because their medical records were not available for review. Of the 24 reviewed, 8 (33.3%) would have de-escalation in antibiotic therapy. Eight (33.3%) would have no change in therapy and 8 (33.3%) could have inappropriate escalation of antibiotics due to reporting of potential pathogens by the PP but recorded as normal flora by cultures.
Conclusion. The use of PP would lead to a reduction of unnecessary antimicrobial therapy in 1/3 of the patients examined. However, quantification of organisms otherwise reported as normal flora may lead to unnecessary treatment and requires education of staff to understand the results of the assay.
Disclosures. No reported disclosures.

642. Higher Diagnostic Accuracy with Ultrasensitive Detection of Helicobacter pylori Stool Antigen Using Single-Molecule Counting Technology
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Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM
Background. Current diagnostic methods for Helicobacter pylori infection include fecal antigen tests. C-urea breath test, and gastric biopsy. The breath test is limited by poor specificity and the fecal antigen tests by poor sensitivity. We have developed a prototype assay for detection of H. pylori antigen in human stool, powered by ultrasensitive Single Molecule Counting technology, and compared the analytical performance to a commercially available enzyme-linked immunosassay (ELISA) antigen test.
Methods. The Singulex Clarity H. pylori antigen assay incubates diluted stool with capture and fluorescent-labeled detection antibodies. After incubation and wash antigen test.
Results. Clinical performance was evaluated using two cohorts, one had 10 ELISA-negative and 10 ELISA-positive samples and the other 13 high positives (> 0.500 at 450/630) and 5 low positives near the ELISA cutoff (0.100–0.500 at 450/630). One sample was excluded due to discordant ELA results, and three to reader flags.
Conclusion. The lower limit of detection of the Clarity H. pylori assay was 1.7 ng/mL and the ELISA 1.250 ng/mL (IFU: LOD 4.67 ng/mL). A high positive stool sample was detectable by the Clarity H. pylori assay diluted 1:10,000,000 and by the ELISA 1:10,000. The Clarity H. pylori assay showed a 729-fold increase in lower limit of detection and 1,000-fold increase in endogenous antigen lower limit of detection compared with the ELISA. Clarity signal ranged from 46–665 DE for ELISA-negative samples and 487,484–576,747 DE for ELISA-positive samples.
Conclusion. The Singulex Clarity H. pylori antigen assay may have orders of magnitude higher sensitivity than the commercial ELA and demonstrated 100% positive agreement and 100% negative agreement on detection of H. pylori antigen in human stool samples. The ultrasensitive Clarity H. pylori assay has the potential for high sensitivity and specificity to improve current diagnostic options for H. pylori infection; however, additional multicenter studies are required.
Disclosures. No reported disclosures.

643. Comparison of Multiplex Polymerase Chain Reaction (PCR) and Routine Culture for the Detection of Respiratory Pathogens in Pneumonia Patients
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Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM
Background. The identification of causative pathogens in pneumonia can be challenging, and conventional culture methods can take up to 72 hours. However, rapid molecular tests identify organisms within hours. The Biofire FilmArray (bioMérieux, North Carolina) Pneumonia Panel was recently approved by the FDA. The multiplex PCR system identifies 33 targets from sputum and bronchoalveolar (BAL) samples, which include 18 bacteria, 8 viruses, and 7 antibiotic resistance genes.
Methods. A retrospective evaluation was performed to compare the panel to routine culture methods for the detection of respiratory pathogens in patients with pneumonia in a 794-bed teaching hospital in northeast Ohio.
Results. One sample was excluded. Twelve cultures were performed using the laboratory's standard procedure, and Pneumonia Panel testing was performed according to manufacturer instructions. The Singulex Clarity H. pylori antigen assay may have orders of magnitude higher sensitivity than the commercial ELA and demonstrated 100% positive agreement and 100% negative agreement on detection of H. pylori antigen in human stool samples. The ultrasensitive Clarity H. pylori assay has the potential for high sensitivity and specificity to improve current diagnostic options for H. pylori infection; however, additional multicenter studies are required.
Disclosures. No reported disclosures.

644. Comparative Evaluation of ETEST® ERV bioMérieux with the CLSI Broth Microdilution Method for Eravacycline MIC Determination
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Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM
Background. Eravacycline (XERAVA®) is a novel, FDA and EMA-approved fully-synthetic fluorocycline antibiotic developed by Tetraphase Pharmaceuticals Inc. for the treatment of complicated intra-abdominal infections (cIAI) including those caused by multidrug-resistant (MDR) pathogens that have been highlighted as urgent public health threats by the US-CDC and the WHO.
Results. The new ETEST ERV strip (MIC range 0.002 – 32 µg/mL) has been developed by bioMérieux and calibrated vs. the broth microdilution reference method (BMD) as described by the Clinical and Laboratory Standards Institute (CLSI) to determine the minimal inhibitory concentration (MIC) of eravacycline against Enterobacterales and Enterococci. The aim of the study was to compare ETEST ERV to the CLSI BMD method on a panel of 166 strains comprising 131 Enterobacteriales and 35 Enterococci.
Methods. Quality control was performed with the CLSI QC strains E.coli ATCC 25922 and E.faecalis ATCC 29212. The ETEST ERV strip was applied on a Mueller–Hinton agar plate previously seeded with a 0.5 McF bacterial suspension. After incubation for 16–20H at 35°C, the reading was performed using the bacteriostatic mode, i.e.,80% of growth. The FDA-approved breakpoints were applied (≤0.5µg/mL for Enterobacteriales and ≤0.064 µg/mL for Enterococci).
Results. The MIC essential agreement was 99.4% at ≤1 dilution for the whole panel and the category agreement was 98.4% with 4.8% Major Errors (1 E. coli, 2 K. pneumoniae, 1 K. aerogenes, 1 C. koseri, 1 E. faecalis), all at ≤1 dilution around the single breakpoint. No Very Major Error (VME) was observed.
Conclusion. In this study, the new ETEST ERV strip has been found to be substantially equivalent to the CLSI reference method. MIC end-points appear easier to read in comparison to the reference method. With a 15-dilution MIC range and simplicity of use, ETEST ERV could represent a valuable tool for MIC determination and an alternative to the BMD reference method. ETEST ERV will undergo clinical studies to seek FDA clearance and CE marking. For Research Use Only. The performance characteristics of this product have not yet been established.
Disclosures. No reported disclosures.

645. Singulex Clarity Norovirus Assay (In Development) Provides Ultrasensitive Detection of Norovirus Genogroups I and II
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Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM
Background. The identification of causative pathogens in pneumonia can be challenging, and conventional culture methods can take up to 72 hours. However, rapid molecular tests identify organisms within hours. The Biofire FilmArray (bioMérieux, North Carolina) Pneumonia Panel was recently approved by the FDA. The multiplex PCR system identifies 33 targets from sputum and bronchoalveolar (BAL) samples, which include 18 bacteria, 8 viruses, and 7 antibiotic resistance genes.
Antibody pairs tested and detected all 19 tested genotypes. The Clarity assay may offer (3) 39 samples negative by a lab-developed test using Cepheid reagents (SmartCycler®). Positive and 5 samples negative by the BioFire positive (19 different genotypes) and 15 were negative by the CDC assay, (2) 3 samples Samples were sourced from three providers: (1) 90 genotyped samples of which 75 were evaluated by testing 137 stool samples from patients with suspected norovirus infection. The Singulex Clarity norovirus assay is currently in development for use on the Singulex Clarity system (Singulex Inc., Alameda, CA, USA), a fully-automated system (Singulex Inc., Alameda, CA, USA), a fully-automated platform powered by Single Molecule Counting technology (registered with the FDA and CE marked). The assay uses paramagnetic microparticles bound to capture antibody and a fluorescence-labeled reporter antibody to detect virion capsid protein of norovirus genogroups I (GI) and II (GII) in the stool. For the development of Clarity Norovirus assay, diagnostic performance of 4 antibody pairs (as Capture and Detection reagent) were evaluated by testing 137 stool samples from patients with suspected norovirus infection. Samples were sourced from three providers: (1) 90 genotyped samples of which 75 were positive (19 different genotypes) and 15 were negative by the CDC assay, (2) 3 samples positive and 5 samples negative by the BioFire FilmArray Gastrointestinal Panel, and (3) 39 samples negative by a lab-developed test using Cepheid reagents (SmartCycler®). From all the antibody pairs tested, one of the pairs had best performance with the area under the receiver operating characteristic (AuROC) curve demonstrating a C-Statistic of 0.959 (95% CI 0.921–0.997), compared with AuROC C-statistic of 0.943 (95% CI 0.896–0.990), 0.871 (95% CI 0.807–0.936), and 0.914 (95% CI 0.863–0.964) for the three other pairs. The Clarity assay detected all 19 different genotypes tested (figures).

Conclusion. The ultrasensitive and rapid Clarity norovirus assay (in development) for detection of GI and GII demonstrated excellent performance with one of the antibody pairs tested and detected all 19 tested genotypes. The Clarity assay may offer a standalone solution for norovirus diagnostics.

Disclosures. All authors: No reported disclosures.

647. Diagnoses Associated with Temperature ≥104°F in Adults

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Session: 67. New Diagnostics

Background. Temperature ≥104°F (T ≥ 104) is uncommon in adults. The diagnoses and clinical characteristics were reviewed for patients with T ≥ 104.

Methods. Infectious disease physicians reviewed charts of patients with T ≥ 104 seen at the Washington DC Veterans Affairs Medical Center from 2009 to 2018. The following was collected: demographics, past medical history, medications, WBC, maximum temperature, time to defervescence, etiology of T ≥ 104, and death.

Results. Less than 0.01% of all patient encounters were associated with T ≥ 104. Of the 60 most recent patients with T ≥ 104 (from 2014 to 2018), the median age was 63.5 years (range 23–97), 65% were African American, 88% were male. 82% of those with T ≥ 104 were hospitalized; 76% of those had the T ≥ 104 on or within 72 hours of admission. 25% of the 60 patients had underlying cancer, 10% HIV, 30% DM, 13% CKD, and 13% were on steroids/imunosuppressants/biologics. The median peak temperature was 104.3°F (interquartile range 104.0 – 104.7), maximum was 106.0°F. 82% had T ≥ 104 for only 1 day and the median time to defervescence was 2 days. There were 55 diagnoses amongst 48 patients; 12 had no identifiable etiology of T ≥ 104. Of the identifiable diagnoses, there were 45 (81.8%) infections, 4 (7.3%) metastatic malignancies (1 Hodgkin’s lymphoma, 1 small cell carcinoma, 1 squamous cell carcinoma, 1 unknown primary), 2 (3.6%) intracranial bleeds, 2 (3.6%) GI bleeds, 1 (1.8%) mixed collagen vascular disease, and 1 (1.8%) neurologic malignant syndrome. The most common infections were 1.5 cases of pneumonia including 2 Legionella, 8 complicated UTI/pyelonephritis, 3 primary bacteremia, 2 West Nile virus, 2 influenza, and 2 cholangitis with bac- teremia. The median WBC of infectious diagnoses (9.8) was significantly higher than noninfectious diagnoses (5.8, P = 0.006, T-test). Of the 60 patients, 28% died within 30 days of T ≥ 104 including 2 patients who died of sepsis. 67% of those who died were receiving hospice care.

Conclusion. T ≥ 104 is rare in adults and is usually associated with bacterial infections such as pneumonia (including Legionella), complicated UTIs/pyelonephritis, and primary bacteremia but may also be seen with viral infections such as West Nile virus and influenza. Mortality is high.

Disclosures. All authors: No reported disclosures.