Session: 152. Host Responses to Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. Chronic obstructive pulmonary disease (COPD) exacerbation and community-acquired pneumonia (CAP) are major drivers of antibiotic overuse, primarily due to challenges in pathogen identification. Pneumococcal and Haemophilus influenzae pneumonia (HiPn) are common pathogens during these events. COPD exacerbation is a major cause of respiratory-related hospital readmission within 30 days of discharge, and antibiotic overuse can lead to several adverse outcomes, including increased hospitalization rates and death within 30 days. A patient’s individual risk profile is essential in determining the need for antibiotic therapy and ensuring appropriate initiation and duration of therapy.

Methods. In this quasi-experimental study, we compared antibiotic use and clinical outcomes in patients with COPD exacerbation and/or CAP treated for COPD exacerbation and/or CAP on primary care clinic visits. The study was conducted at Mercy Medical Center in Canton, Ohio, during the months of September 2017 through January 2018. The primary outcome was antibiotic use, defined as the number of antibiotic prescriptions filled within 30 days of discharge. Secondary outcomes included all-cause hospital readmission within 30 days of discharge, respiratory-related hospital readmission within 30 days of discharge, 30-day mortality, hospital length of stay, and adverse events to antibiotics.

Results. A total of 76 patients were included in the study, 43 in the control group and 33 in the PCT group. Baseline characteristics were similar between groups. The use of a PCT algorithm significantly decreased duration of antibiotics by 2.7 days in comparison to the control group and resulted in a significant decrease in antibiotic use by 2.7 days. Secondary safety outcomes between the PCT and control group were similar, including all-cause hospital readmission within 30 days of discharge (30.3% vs. 25.6%; P = 0.648), and respiratory-related hospital readmission within 30 days of discharge (80.0% vs. 81.8%; P = 0.731), and 30-day mortality (no incidence in either group).

Conclusion. The use of a PCT algorithm significantly reduced duration of antibiotics by 2.7 days without negatively impacting clinical outcomes in patients being treated for COPD exacerbation and/or CAP.

Length of Antibiotic Therapy

| Mean Antibiotic-Days (SD) | 95% CI (p<0.001) |
|---------------------------|------------------|
| Control (n=43)            | 5.3 (3.5)        |
| PCT (n=33)                | 2.6 (2.55)       |

Disclosures. All authors: No reported disclosures.

1338. Development of a Novel Application for Differential Diagnosis of Tick-borne Diseases
Corey Meyer, PhD; Jaleel Sanjoh, PhD; Audrey Cerles; Christian Garnier; Laurel MacMillan, MS; Gryphon Scientific, Takoma Park, Maryland
Session: 152. Host Responses to Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. Early diagnosis and treatment of tick-borne diseases ( TBDs ) is critical for mitigating their adverse health outcomes, but the differential diagnosis of TBDs is challenging because many symptoms are nonspecific and commonly used diagnostic assays have significant shortcomings. Furthermore, although the local incidence of TBDs is recognized as an important factor in diagnosis, tools to help clinicians formally consider surveillance data in their decision-making are not available. To address these gaps, Gryphon Scientific developed a differential diagnosis application (app) for TBDs that calculates a patient’s likelihood of infection with specific TBDs based on their symptoms, risk factors, and state of suspected tick exposure.

Methods. A differential diagnosis model for TBDs was developed using data on: 1) TBD symptom and risk factor prevalence in TBD patient populations, collected from clinical studies; and 2) human TBD incidence data from notifiable disease surveillance systems and tick infection prevalence data from reports and public databases, which were combined to develop an environmental risk measure. These data were used to build a Bayesian Belief Network (BBN) model that predicts TBD infection probabilities based on a patient’s symptoms, risk factors, and state of suspected tick exposure. The model was validated using case studies from the biomedical literature. The model was incorporated into an app developed using R-shiny, called TBD-DDx (Figures 1 and 3).

Results. A pilot application was developed that includes 10 states (AR, CT, MA, ME, MN, MO, NH, RI, VT, and WI) and the 11 TBDs endemic to those states. The differential diagnosis model identified the patient’s true disease as the top-predicted disease in 56% of cases and within the top three predicted TBD in 84% of cases. The inclusion of incidence factors in the model improved performance (Figure 4).

Conclusion. These results demonstrate that the TBD-DDx app is a promising tool for informing clinical diagnoses of TBDs to guide selection of diagnostic testing and treatment. This study represents the first use of a BBN modeling approach that incorporates an environmental risk measure in the differential diagnosis of other diseases with environmental or other exposure risks.

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Background. Opsonophagocytic assays (OPAs) are an important tool for assessing vaccine-induced functional antibody responses. OPAs are complex assays composed of many biological components (eg serum, complement sources, bacteria, and human phagocytes) which contribute to assay variability and may result in titr dilution if not carefully controlled. Rigorous development and validation coupled with robust assays have significant shortcomings. Furthermore, although the local incidence of pneumococcal conjugate vaccines such as 20vPnC, whose licensure depends on demonstration of non-inferiority to 13vPnC.

Conclusion. Maintenance and careful monitoring of high-quality assays to measure functional antibody responses, such as OPAs, is critical for the delivery of reliable serological data to support the advancement of pneumococcal vaccine programs. Pneumococcal OPAs must be rigorously maintained to ensure continuity of serological data over time and inform licensure decisions of next-generation vaccines as well as postmarketing and seroepidemiology studies.

Disclosures. All authors: No reported disclosures.
1339. Impact of Implementing Procalcitonin Testing with Comprehensive Education on Procalcitonin Ordering Habits and Antibiotic Usage
Joyce Johnsrud, MD; Ryan K. Dare, MD, MS; University of Arkansas for Medical Sciences, Little Rock, Arkansas
Session: 152. Host Responses to Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. Procalcitonin (PCT) has emerged as a biomarker distinguishing bacterial from non-bacterial infections with FDA approval for acute respiratory infections and sepsis. Studies show that PCT use can reduce patient harm while decreasing antibiotic usage. Our objective was to evaluate PCT use at our hospital and assess the impact of a comprehensive education intervention.

Methods. In-house PCT testing was implemented at our institution April 2018 along with a rigorous education campaign. Interventions consisted of face-to-face didactics with 5 provider groups, distribution of evidence-based interpretation algorithms, development of EMR prompts to guide appropriate ordering, and creation of syndrome-specific interpretation displayed as PCT results. Retrospective analysis comparing pre-intervention (December 2017) to post-intervention (October 2018) was performed evaluating ordering habits and impact of PCT result on antibiotic management. Statistical analysis was performed using STATA 14.2.

Results. 218 PCT orders from 170 patients and 263 PCT orders from 170 patients were included in the pre- and post-intervention periods, respectively. All provider groups who received face-to-face education changed their antibiotic management. Statistical analysis was performed using STATA 14.2.

Conclusions. Providing comprehensive PCT education significantly impacted PCT ordering habits. Testing improved ability to comply with FDA-approved indications, specifically in providers who received face-to-face education. Appropriate alteration of therapy based on PCT results were similar between groups suggesting repeat education is needed to avoid confirmation bias.

Disclosures. All authors: No reported disclosures.

1340. The Effect of Continuous Renal Replacement Therapy on Body Temperature in Patients with and without Infection
Douglas W. Challener, MD; Kamosh Ashani, MD, MS; John C. O’Horo, Sr, MD, MPH; Mayo Clinic, Rochester, Minnesota
Session: 152. Host Responses to Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. Sepsis frequently leads to acute kidney injury. In severe cases, patients may require continuous renal replacement therapy (CRRT) which involves placement of a dialysis catheter and an extravascular blood filtration circuit. CRRT is commonly considered to “mask” fever, though this phenomenon has not been investigated.

Methods. We queried an institutional database of all patients on CRRT from 2007 to 2015 for inpatient temperature data and antibiotic administration records. Receipts of piperacillin–tazobactam, a carbapenem, or a third or fourth-generation cephalosporin, indicating a serious infection, were considered intervention arm. We analyzed temperatures recorded in the intensive care unit before, during, and after CRRT. Patients were divided into groups that did not receive antibiotics as well as those who did. Temperature data were Winsorized to correct for outliers. We also performed descriptive statistics for each group.

Results. There were 3,379,988 temperature readings for 1,568 ICU patients on CRRT. 1,153 patients received broad-spectrum antibiotics in ICU. In patients who received antibiotics in ICU and were presumed to have an infection, the mean temperature was 37.2°C prior to initiation of CRRT, 36.4°C while on CRRT, and 37.2°C following discontinuation of CRRT. In the 415 patients who did not receive IV antibiotics, the mean temperature was 36.9°C prior to initiation of CRRT, 36.6°C while on CRRT, and 37.0°C following discontinuation of CRRT. During each of the periods before, during, and after CRRT, patients who received antibiotics had significantly higher temperatures than those who did not (P < 0.001). Patients receiving antibiotics were generally younger (mean 60 years vs. 64 years, P < 0.001), had longer ICU stays (mean 29 days vs. 12 days, P < 0.001) and spent more time being ventilated (mean 23 days vs. 7 days, P < 0.001). The mean SOFA score on day one was similar (mean 11.1 in the antibiotic group and 10.5 in the other group).

Conclusions. This investigation suggests that patients have slightly lower temperatures while on CRRT, by on average less than half a degree. A similar effect is seen in both patients with infections as well as those without. Further work will be needed to determine what constitutes a true febrile response in this population.

Disclosures. All authors: No reported disclosures.

1341. Development of a Series of High-Throughput Screens to Identify Leads for Nontuberculous Mycobacteria Drug Design
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Session: 153. Mycobacteria
Friday, October 4, 2019: 12:15 PM

Background. Nontuberculous mycobacteria (NTM), particularly Mycobacterium avium complex and Mycobacterium abscessus complex, cause significant morbidity and mortality in patients with impaired host immunity or pre-existing structural lung conditions. NTM infections are increasing at an alarming rate worldwide and there is a dearth of progress in regard to the development of efficacious and tolerable drugs to treat such infections. Traditional drug discovery screens do not account for the diverse physiologic conditions, microenvironments, and compartments that the bacillus encounters during human infection. In order to help populate the NTM drug pipeline, and explore the disconnect between in vitro activity, in vivo activity; and clinical outcomes, we are developing a high throughput in vitro assay platform that will more closely model the unique infection-related conditions encountered by NTM.

Methods. We are developing and validating a suite of in vitro assays that screen compounds for activity against extracellular planktonic bacteria, extracellular bacteria within biofilms, intracellular bacteria, and nutrient-starved non-replicating bacteria. We are using both the smooth and rough morphtype of NTM for these tests.

Results. We have validated high throughput assays to pharmaceutical standards for replicating and non-replicating M. abscessus. We have also tested a panel of 18 known anti-mycobacterial compounds. assay development is currently underway to test compounds for activity against NTM in biofilm and inside macrophages as well.

Conclusions. To enhance optimization identification, focusing on the starting points for NTM drug development, focused libraries of compounds that have undergone significant preclinical profiling and/or compounds with known activity against M. tuberculosis (TB) will be screened. Such a ‘piggyback’ approach upsars advances made in TB drug development and leverages them for NTM drug discovery. This will help expedite novel drug development, reduce attrition rate, and offer a shorter route to clinical use as it exploits the prior investment in medicinal chemistry, pharmacology, and toxicology.

Disclosures. All authors: No reported disclosures.

1342. Impact of HIV Infection on Treatment Outcome of New Tuberculosis Patients Attending Tuberculosis and Antiretroviral Treatment Services in the Community-Based Hospital, Thailand: A Retrospective Cohort Study
Subenchana Pinsai, MD; Chao Phraya Abhaibhubejhr Hospital, Muang, Prachin Buri, Thailand
Session: 153. Mycobacteria
Friday, October 4, 2019: 12:15 PM

Background. Tuberculosis (TB) and HIV are one of the significant public health problems in Thailand, and an estimated 15,000 individuals have a dual infection. Both HIV and TB each disease speeds up the progression of each other. TB is the leading complex and mortality in patients with impaired host immunity or pre-existing structural lung conditions. NTM infections are increasing at an alarming rate worldwide and there is a dearth of progress in regard to the development of efficacious and tolerable drugs to treat such infections. Traditional drug discovery screens do not account for the diverse physiologic conditions, microenvironments, and compartments that the bacillus encounters during human infection. In order to help populate the NTM drug pipeline, and explore the disconnect between in vitro activity, in vivo activity; and clinical outcomes, we are developing a high throughput in vitro assay platform that will more closely model the unique infection-related conditions encountered by NTM.

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Douglas W. Challener, MD; Kamosh Ashani, MD, MS; John C. O’Horo, Sr, MD, MPH; Mayo Clinic, Rochester, Minnesota
Session: 152. Host Responses to Diagnostics
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