1334. Performance of C-Reactive Protein and Procalcitonin in Immunocompromised Children with SIRS

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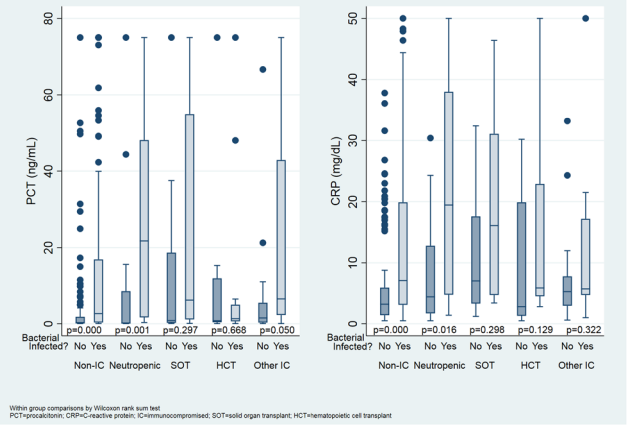
Background. Biomarkers (C-reactive protein [CRP], procalcitonin [PCT]) have been used in patients with systemic inflammatory response syndrome (SIRS) to identify those with and without bacterial infection. However, their performance in immunocompromised (IC) children is not well studied.

Methods. Retrospective chart review of episodes of SIRS in IC children <19 years old admitted to the PICU August 2012–June 2016 with: (a) blood culture, PCT, and CRP obtained within 6 hours of SIRS, (b) no recent SIRS episodes (> 30 days), and (c) no positive blood culture in 2 days preceding SIRS. We defined IC as neutropenia (ANC< 500), solid-organ transplant (SOT), hematopoietic cell transplant (HCT), and other (immunosuppressive medications or primary immunodeficiency). To identify a comparator group, we additionally reviewed a previously published cohort of non-IC children with SIRS (Downes, et al, JPIDS 2018), applying the same inclusion criteria. For each episode (first 48 hours after SIRS), we determined the presence of bacterial infection using NHSN definitions and viral infection as symptoms with positive PCR. We compared biomarkers in IC children with and without bacterial infection, and in IC and non-IC children, using Wilcoxon rank-sum tests.

Results. We identified 108 SIRS episodes in 94 IC children (neutropenia = 35, SOT = 18, HCT = 22, other = 33) and 278 episodes in 250 non-IC children. Age (P = 0.15) and gender (P = 0.70) were similar among IC and non-IC groups. 41% of episodes in both IC and non-IC children had bacterial infections (P = 0.96). PCT and CRP were significantly higher in IC children with bacterial infection than those without (Figure 1). Biomarkers did not differ significantly among episodes in IC and non-IC children with bacterial infection; however, among episodes without bacterial infection, biomarkers were higher in IC than non-IC children (Table 1). Detection of a viral infection did not affect biomarker values in IC or non-IC children when bacterial infection was absent (Table 2).

Conclusion. In IC children with SIRS, PCT and CRP were higher when bacterial infection was present. Meanwhile, in the subset of non-bacterial SIRS episodes, biomarkers were higher in IC compared with non-IC children. PCT and CRP may be valuable markers to discriminate bacterial from non-bacterial causes of SIRS in IC children.

Figure 1: Box Plots of PCT and CRP for Bacterial Infected vs Uninfected by Group



Within group comparisons by Wilcoxon rank sum test
PCT=procalcitonin; CRP=C-reactive protein; IC=immunocompromised; SOT=solid organ transplant; HCT=hematopoietic cell transplant

Table 1: Biomarkers in IC vs Non-IC Patients Based on the Presence of Bacterial Infection

Group	PCT (ng/mL), median (IQR)			CRP (mg/dL), median (IQR)		
	Bacterial infection present	Bacterial infection absent	p-value[a]	Bacterial infection present	Bacterial infection absent	p-value[a]
Non-IC (n=278)	2.67 (0.32-16.91)	0.32 (0.09-1.83)	0.000	7.05 (3.10-19.90)	3.20 (1.40-5.90)	0.000
All IC (n=108)	4.85 (1.02-43.16)	0.79 (0.20-7.74)	0.001	7.85 (4.70-25.70)	4.95 (2.20-12.40)	0.002
p-value[b]	0.063	0.008	--	0.086	0.006	--

All biomarker values reported as median (IQR). PCT=procalcitonin, CRP=C-reactive protein, IC=immunocompromised
[a]Wilcoxon rank sum tests used for comparison of within group biomarkers based on presence or absence of bacterial infection
[b]Wilcoxon rank sum tests used for comparison of biomarkers between IC and non-IC groups with same bacterial infection status

Table 2: Biomarkers in the Subset of Patients Without Bacterial Infection Based on Presence of Viral Infection

Group	PCT (ng/mL), median (IQR)			CRP (mg/dL), median (IQR)		
	Viral infection detected	Viral infection not detected	p-value[a]	Viral infection detected	Viral infection not detected	p-value[a]
Non-IC (n=164)	0.30 (0.08-2.90)	0.33 (0.11-1.47)	0.765	2.90 (1.65-4.80)	3.50 (0.95-8.20)	0.277
All IC (n=64)	0.77 (0.20-15.33)	0.80 (0.20-7.52)	0.881	5.10 (2.10-8.70)	4.80 (2.30-12.80)	0.953
p-value[b]	0.233	0.019	--	0.111	0.089	--

All biomarker values reported as median (IQR). PCT=procalcitonin, CRP=C-reactive protein, IC=immunocompromised
[a]Wilcoxon rank sum tests used for comparison of within group biomarkers based on presence or absence of viral infection
[b]Wilcoxon rank sum tests used for comparison of biomarkers between IC and non-IC groups with same viral infection status

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1335. A Translational Nephrotoxicity Model to Probe Acute Kidney Injury with Vancomycin and Piperacillin–Tazobactam

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Background. Vancomycin and piperacillin–tazobactam (VAN+TZP) are two of the most commonly utilized antibiotics in the hospital setting and are reported in clinical studies to increase acute kidney injury (AKI). However, no clinical study has demonstrated that synergistic AKI occurs, only that serum creatinine increases with VAN+TZP. Previous preclinical work demonstrated that novel urinary biomarkers and histopathologic scores were not increased in the VAN+TZP group compared with VAN alone. The purpose of this study was to assess changes in urinary output and plasma creatinine between VAN, TZP, and VAN+TZP treatments.

Methods. Male Sprague–Dawley rats (n = 32) received either saline, VAN 150 mg/kg/day intravenously, TZP 1,400 mg/kg/day intraperitoneally, or VAN+TZP for 3 days. Animals were placed in metabolic cages pre-study and on drug dosing days 1–3. Urinary output, plasma creatinine, urinary biomarkers were compared daily and kidney histopathology was compared at the end of therapy between the groups. Mixed-effects, repeated-measures models were employed to assess differences between the groups.

Results. In the VAN-treated rats, urinary output was increased on days 1, 2 and 3 compared with baseline and saline ($P < 0.01$ for all), whereas it increased later for VAN+TZP (i.e., day 2 and 3 compared with saline, $P < 0.001$). No changes in urinary output were observed with saline and TZP alone. Plasma creatinine rose for VAN on days 1, 2, and 3 from baseline and VAN+TZP on day 3 ($P < 0.02$ for all), but no treatment group was different from saline. In the VAN-treated rats, urinary KIM-1 and clusterin were increased on days 1, 2, and 3 compared with controls ($P < 0.001$). Elevations were seen only after 3 days of treatment with VAN+TZP ($P < 0.001$ KIM-1, $P < 0.05$ clusterin). No changes in urinary biomarkers output were observed with saline and TZP alone. Histopathology was only elevated in the VAN group compared with saline ($P < 0.002$). No histopathology changes were noted with VAN+TZP.

Conclusion. All groups with VAN demonstrated kidney injury; however, VAN+TZP did not cause more kidney injury than VAN alone in a rat model of VIKI when using plasma creatinine, urinary output, or urinary biomarkers as outcomes. Histopathology data suggest that adding TZP did not worsen VAN-induced AKI and may even be protective.

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1336. Impact of Procalcitonin-Guided Antibiotic Management in Chronic Obstructive Pulmonary Disease Exacerbation and Community-Acquired Pneumonia

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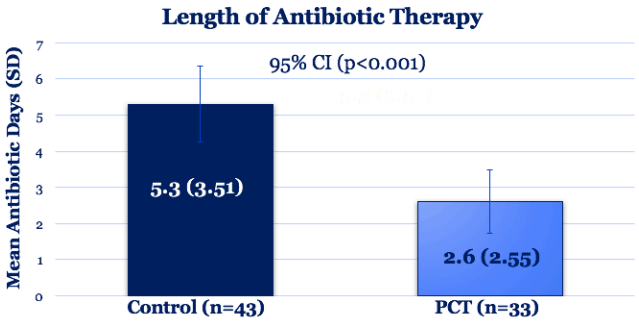
Background. Chronic obstructive pulmonary disease (COPD) exacerbation and community-acquired pneumonia (CAP) are major drivers of antibiotic overuse, primarily due to challenges in pathogen identification. Procalcitonin is a serum biomarker that assists in distinguishing bacterial infection from other causes. The purpose of this study was to determine whether the use of a procalcitonin (PCT) guided algorithm in patients diagnosed with COPD exacerbation and/or CAP can reduce antibiotic exposure without negatively impacting clinical outcomes.

Methods. This was a quasi-experimental study conducted at Mercy Medical Center in Canton, Ohio. The patient data for the retrospective cohort (control group) was collected from the months of September 2017 through January 2018. The prospective phase (PCT group) took place during the months of September 2018 through January 2019. Physicians utilized a procalcitonin guided algorithm to determine appropriate initiation and duration of antibiotic use in patients admitted with a primary diagnosis of COPD exacerbation and/or CAP. The primary outcome was the duration of antibiotic therapy, measured in days. 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 (2.6 [$n = 33$] vs. 5.3 [$n = 43$] days; $P < 0.001$; 95% CI). 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%; $P = 0.648$), respiratory-related hospital readmission within 30 days of discharge (80.0% [$n = 10$] vs. 81.8% [$n = 11$]; $P = 0.731$), 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.



Disclosures. **All authors:** No reported disclosures.

1337. Development, Maintenance, and Application of Opsonophagocytic Assays to Measure Functional Antibody Responses to Support a 20 Valent Pneumococcal Conjugate Vaccine

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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 titer drift if not carefully controlled. Rigorous development and validation coupled with routine monitoring of assay performance are required to ensure that high-quality OPA serological data are consistently generated throughout the lifetime of existing and next-generation pneumococcal vaccines.

Methods. OPA specificity was demonstrated by competing functional antibody activity with pneumococcal polysaccharides. Assay qualification/validation assessed accuracy, precision, and sample linearity. Assay performance over time was assessed through the implementation of quality control serum data tracking systems and longterm serum proficiency panels that are routinely tested during assay performance. Human quality control sera are included on each assay plate to ensure that each plate meets pre-specified acceptance criteria. Proficiency serum panels are comprised of individual human serum samples derived from subjects immunized with pneumococcal vaccines and are used to monitor performance across a range of serological titers and over time.

Results. The OPAs were shown to be specific and reproducible. Monitoring of assay performance over time demonstrated that the assays are stable. For the 13 serotypes contained in 13vPnC reliable titers have been generated in over a decade of testing which is an essential prerequisite in the evaluation of next-generation 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.

1338. Development of a Novel Application for Differential Diagnosis of Tick-borne Diseases

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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. Performance of 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 and could be adapted for differential diagnosis of other diseases with environmental or other exposure risks.