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1538. Evaluation of a 15-valent Pneumococcal Conjugate Vaccine in an Adult Rhesus Macaque Immunogenicity Model

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Background. *Streptococcus pneumoniae* (pneumococcus) is a leading cause of a variety of diseases, including bacteremia, meningitis, and pneumonia, among older adults in the United States. Immunization with pneumococcal vaccines is an effective way to prevent these diseases. In this study, we evaluated the immunogenicity of 15-valent pneumococcal conjugate vaccine (PCV15) in adult rhesus macaques.

Methods. Animals were intramuscularly immunized with PNEUMOVAX® 23 and PCV15 vaccine (5 animals/group) and sera were collected before immunization and 30, 60, and 90 days after the immunization. Sera were assayed using multiplexed electrochemiluminescent (ECL) assays to measure serotype-specific IgG antibodies to all vaccine serotypes and multiplexed opsonophagocytic killing assays (MOPA) to measure functional antibody responses to 15 vaccine serotypes.

Results. At day 30 post immunization, 16 out of the 23 serotypes in PNEUMOVAX 23 groups induced statistically significant higher ECL titers compared with pre bleed, ranging from 1.6-fold (19A) to 28.3-fold (15B). Compared with PNEUMOVAX 23, PCV15 induced much higher ECL titers. Thirteen out of the 15 serotypes in PCV15 groups induced statistically significant higher ECL titers compared with pre bleed, ranging from 7.4-fold (14) to 47.3-fold (4). The ECL antibody titers gradually decreased from day 30 to day 90 for both groups. We also compared the functional MOPA titers of the day 30 sera compared with pre bleed for 15 vaccine serotypes. Out of the 14 common vaccine serotypes, 7 serotypes in the PNEUMOVAX 23 immunized macaques had a >4 fold increase in MOPA titer, ranging from 4-fold (22F) to 3902-fold (33F) and 11 serotypes in the PCV15 immunized macaques had a >4-fold increase in MOPA titer, ranging from 6.3-fold (23F) to 4445-fold (7F). Twelve out of the 14 common serotypes in PCV15 group had higher MOPA titers compared with the PNEUMOVAX 23 group, although they didn't reach statistical significance due to high variability.

Conclusion. These data demonstrate that a single dose of PCV15 is highly immunogenic in adult rhesus macaques and has better immunogenicity for most common serotypes compared with PNEUMOVAX 23. However, PNEUMOVAX 23 offers broader serotype coverage with 9 additional serotypes contained in the vaccine.

Disclosures. **J. Xie**, Merck & Co. Inc: Employee, Salary; **R. Kaufhold**, Merck & Co. Inc: Employee, Salary; **D. Mcguinness**, Merck & Co. Inc: Employee, Salary; **Y. Zhang**, Merck & Co. Inc.: Employee, Salary; **W. Smith**, Merck & Co. Inc.: Employee, Salary; **C. Giovarelli**, Merck & Co. Inc.: Employee, Salary; **M. Winters**, Merck & Co. Inc: Employee, Salary; **L. Musey**, Merck & Co. Inc: Employee, Salary; **M. Kosinski**, Merck & Co. Inc: Employee, Salary; **J. Skinner**, Merck & Co. Inc: Employee, Salary

1539. Foley Catheter with Peri-Urethral Antimicrobial Irrigation for the Prevention of Catheter Associated Urinary Tract Infections – Assessment in an *In Vitro* Model

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Background. Catheter associated urinary tract infections (CAUTIs) are a significant medical issue with substantial morbidities and costs. CAUTIs are primarily caused by colonization of the external surface of Foley catheters which serve as conduits for colonizing microbes to access the bladder. In order to prevent these CAUTIs, we developed a double-cuff Foley catheter with a novel irrigation cuff for daily irrigation of the periurethral space with a biocompatible antimicrobial disinfecting solution. This study assessed the efficacy of this system for reducing external-surface microbial colonization of catheters in an in vitro model.

Methods. The novel double cuff Foley and disinfectant solutions were evaluated in an established *in vitro* CAUTI model (Gaonkar, et al 2003) where a Foley catheter indwelled in a simulated urethra. 5.5×10^5 CFU of common uropathogens (MRSA, *E. coli*, *C. albicans*) were allowed to attach to the external catheter surface at meatal end of the catheter for 2 hours at 37°C. Subsequently, 3 mL of disinfectant solutions were instilled through the irrigation cuff and covered the periurethral catheter surfaces. Catheters were then incubated an additional 24–48 hours at 37°C, removed, cut into segments, and adherent organisms were quantified by sonication. Disinfectant solutions evaluated included various combinations of 1% polygalacturonic acid (PG), 0.4% caprylic acid (CAP) and (dilute) 0.3% H_2O_2.

Results. For all organisms tested only the triple combination periurtehral flush (PG+CAP+H_2O_2) completely prevented biofilm colonization of catheters indicating antimicrobial synergy of the component agents. Control catheters grew $>10^4$ CFU/segment. Single agent or double agents combinations were only partially effective in preventing colonization by all three pathogens.

Conclusion. The PG + CAP + H_2O_2 periurethral disinfectant flush instilled through an irrigation cuff in a novel double-cuff Foley catheter was able to completely prevent microbial colonization of the external catheter surface by *MRSA, E. coli and C. albicans* in an in vitro CAUTI model. In vivo studies are needed to further evaluate this technology for prevention of CAUTI.

Disclosures. **J. Rosenblatt**, Infective Technologies, LLC: Co-Inventor of the Nitroglycerin-Citrate-Ethanol catheter lock solution technology which is owned by the University of Texas MD Anderson Cancer Center (UTMDACC) and has been licensed by Novel Anti-Infective Technologies, LLC in which Dr. Rosenblatt is a and Shareholder, Licensing agreement or royalty; UT MD Anderson Cancer Center: Co-Inventor of the Nitroglycerin-Citrate-Ethanol catheter lock solution technology which is owned by the University of Texas MD Anderson Cancer Center (UTMDACC) and has been licensed by Novel Anti-Infective Technologies, LLC in which Dr. Rosenblatt is a s and Scientific Advisor, Licensing agreement or royalty; **I. Raad**, Merck: Grant Investigator, Research grant; Allergan: Grant Investigator, Research grant; Infective Technologies, LLC: Co-Inventor of the Nitroglycerin-Citrate-Ethanol catheter lock solution technology which is owned by the University of Texas MD Anderson Cancer Center (UTMDACC) and has been licensed by Novel Anti-Infective Technologies, LLC in which Dr. Raad is a s and Shareholder, Licensing agreement or royalty

1540. *In Vitro* Characterization of the Neurapheresis™ System for the Treatment of Cryptococcal Meningitis

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Background. Cryptococcal Meningitis (CM) is the most common cause of fungal meningitis in adults. Treatment for CM is an induction, consolidation, and maintenance approach with antifungal agents. but is associated with continued high morbidity and mortality. Here we describe the *in vitro* characterization of a catheter-based extracorporeal filtration system (Neurapheresis™) as an alternative mechanical intervention for the filtration of *C. neoformans* cells, polysaccharide antigen, and inflammatory mediators from infected cerebrospinal fluid (CSF).

Methods. H99, a clinical strain of *C. neoformans*, was grown overnight in YPD before being transferred to diluted Saboraud/MOPS media for 24 hours to induce cell proliferation and capsule growth, respectively. Cells were diluted to clinically relevant concentrations (1×10^7 and 1×10^5 cells/mL) in 150 mL of Saboraud/MOPS and passed through the closed-loop system with either 100 or 5 kDa tangential flow filters. Samples were taken every full CSF volume filtration cycle (150 mL) for quantification of yeast load, antigen, and cytokines. Infected human CSF was used to obtain cytokine data.

Results. Both tangential flow filter sizes thoroughly cleared yeasts. Over 24 cycles, we consistently observed a 5-log drop (≥99%) in colony forming units (CFUs), which resulted in complete elimination at a starting concentration of 1×10^5 cells/mL. Both 100 and 5kDa achieved a substantial antigen reduction (using CrAg LFA [initial titer]-[final titer]; [$1:10^5$]–[$1:10^4$] and [$1:10^5$]–[$1:10^2$], respectively). A similar reduction in cytokine levels (IL-1ra, IL-6, TNF, CRP, and CXCL10) in infected human CSF was also achieved (100 kDa reduced all cytokines except IL-1ra by >95% baseline, and 5kDa removed >95% of all quantified cytokines).

Conclusion. Continuous filtration via Neurapheresis is capable of eliminating CSF CFU burden in an *in vitro* CM model. Future iterations may include adjunctive infusions with drug therapies to further accelerate eradication of yeasts. Significant reduction of cryptococcal antigen and inflammatory cytokines also has potential for controlling the neuro-inflammatory storm that accompanies CM.

Disclosures. **B. Hedstrom**, Minnetronix, Inc.: Employee, Salary; **L. Zitella Verbick**, Minnetronix, Inc.: Employee, Salary; **A. Mccabe**, Minnetronix, Inc.: Employee, Salary; **S. P. Lad**, Minnetronix, Inc.: Collaborator and Scientific Advisor, Licensing agreement or royalty, Research grant and Research support

1541. An Offer You Can't Refuse: Clinical Impact of Accepting or Rejecting a Recommendation from an Antibiotic Stewardship Program

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Background. The outcomes associated with the acceptance or refusal of a recommendation from an antimicrobial stewardship program (ASP) on an individual level have not been studied yet. Our objective was to compare the clinical characteristics and mortality of patients for whom a recommendation from an ASP, based on prospective audit and feedback and triggered by a computerized decision support system, was accepted or refused.

Methods. We performed a retrospective cohort study of all hospitalized adult patients who received intravenous or oral antimicrobials in two tertiary care hospitals in Canada between 2014 and 2016, and for whom a recommendation was issued by an ASP.

Results. We identified 1,251 recommendations throughout the study period. Among the recommendations made by the pharmacist to prescribers, 1,144 (91.5%) were accepted. The most frequent interventions were immediate scheduling end of treatment (n = 364, 29%), dosing/frequency adjustments (n = 321, 26%), streamlining (n = 251, 20%), and switching from intravenous to oral therapy (n = 247, 20%). The antimicrobials most frequently targeted by recommendations were piperacillin/tazobactam (n = 273, 22%) and fluroquinolones (n = 267, 21). Overall, the length of the antimicrobial targeted by the recommendation was significantly shorter when a recommendation was accepted (0.37 days vs. 2.11 days; $P < .001$). In the multiple logistic regression analysis, the independent risk factors associated with in-hospital mortality were the Charlson score, issuance of a recommendation for a patient in the intensive care unit, the duration between admission and the recommendation, issuance of a recommendation in 2016 (compared with 2014), and age of the patient. A recommendation issued on a fluoroquinolone or oral penicillin/first generation cephalosporin was associated with lower odds of mortality. After adjustment, refusal of a recommendation by the attending physician was associated with a higher, albeit nonsignificant, risk of mortality (AOR, 1.81; 95% CI, 0.89–3.68; $P = .10$).

Conclusion. The duration of the antimicrobial treatment was significantly shorter when a recommendation triggered by an ASP program was accepted. This decrease in antimicrobial duration was not associated with increased mortality.

Disclosures. **J. Perron**, Lumed Inc., the company that commercializes APSS: Shareholder, Shareholder; **V. Nault**, Lumed Inc., the company that commercializes APSS: Shareholder, Shareholder; **M. Beaudoin**, Lumed Inc., the company that commercializes APSS: Shareholder, Shareholder; **L. Valiquette**, Lumed Inc., the company that commercializes APSS: Shareholder, Shareholder

1542. Safety of Stopping Antibiotics Prescribed "Just in Case" – Comparison of Mortality, Readmissions and *Clostridium difficile* in Patients with Accepted Stewardship Interventions Compared with Declined

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Background. Antibiotics are often prescribed "just in case" when clinical conditions mimic an infection, such as the shortness of breath in heart failure, the erythema of venous stasis or when bacterial culture results are misleading such as asymptomatic bacteriuria (ABU) and *C difficile* colonization. Through prospective audit and feedback (PAF), antimicrobial stewardship programs (ASP) may guide providers toward appropriate antibiotic use. However, the safety of stopping antibiotics needs to be assessed. We retrospectively reviewed the clinical outcomes of patients with accepted ASP recommendations and compared these to patients in whom the primary team declined ASP recommendations.

Methods. The ASP database was used to identify patients receiving written PAF to stop antibiotics prescribed for noninfectious conditions from January 1, 2016 to December 31, 2016. The primary objective was to compare antibiotic days of therapy (DOT), total length of therapy (LOT), hospital length of stay (LOS), 30-day mortality, and the incidence of *C. difficile* within 6 months of the ASP intervention, occurring among patients whose primary treating team accepted vs. rejected the ASP recommendation. We compared the two groups using Chi-square and student t-test to determine statistical significance for categorical and continuous variables, respectively.

Results. There were 232 ASP recommendations to stop antibiotics for noninfectious conditions: 150 (65%) interventions were accepted. Baseline demographic characteristics, comorbidities, intensive care admission and surgery during that hospitalization were similar between the two groups. The most common noninfectious conditions were ABU (55%), followed by respiratory (19%) and intra-abdominal (17%). The median antibiotic DOT and LOT were significantly reduced in the accepted group, 3 (3–5) vs. 8 (5–12.25) days ($P < 0.001$) and 3 (2–4) vs. 7 (5–10) days ($P < 0.001$), respectively. There were no statistical differences in 30-day mortality, 30-day readmission, and *C.difficile*within 6 months.

Conclusion. Our institutional ASP's PAF to stop antibiotics for noninfectious conditions led to a significant reduction in antimicrobial exposure without negatively affecting mortality or hospital outcomes.

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

1543. A Multi-Faceted Antimicrobial Stewardship Program (ASP) Intervention Using Clinical Pharmacists Reduces Antibiotic Use and Hospital-Acquired *Clostridium difficile* Infection (HA-CDI)

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Background. ASPs continue to investigate novel ways to improve appropriate antibiotic utilization. The impact of an ASP-led, multi-faceted coaching and real-time feedback model directed towards clinical pharmacists was evaluated.

Methods. A single-center, pre-post quasi-experimental study was conducted with a four-month historical control period (11/2016–2/2017) and four-month intervention period (4/2016–7/2016) to reduce the use of ceftriaxone, fluoroquinolones, and clindamycin. Clinical pharmacists were responsible for ensuring the appropriate use of these restricted antimicrobials with limited guidance by the ASP in the historical control period. The intervention was multi-faceted: ASP pharmacists provided daily coaching and feedback on use of targeted agents to the clinical pharmacists, clinical pharmacists made recommendations to optimize therapy, and in-person monthly sessions were held where a dashboard consisting of aggregated utilization data and HA-CDI rates was discussed by the ASP pharmacist. Segmented regression analysis was used to determine the significance of this intervention on the utilization of the antibiotics, measured by days of therapy (DOT) per 1000 patient-days (PD). Rates of HA-CDI were also compared between the groups.

Results. The use of fluoroquinolones (34.4 vs. 26.2 DOT/1000 PD; Δ -23.9%), ceftriaxone (17.7 vs.. 13.6 DOT/1000 PD; Δ -23.2%), and clindamycin (18.7 vs.. 13.3 DOT/1000 PD; Δ -28.9%) decreased during the intervention period. Using segmented regression analysis, a significant decreasing rate of antibiotic use of all three agents was observed during the intervention period (Table). A significant decreasing rate of HA-CDI was also seen (rate ratio (RR): 0.787, 95% CI: 0.743–0.833, $P < 0.001$).

Conclusion. A multi-faceted coaching and feedback intervention targeting clinical pharmacists with substantial ASP oversight can significantly reduce inappropriate antibiotic use and HA-CDI in a large hospital.

Table: Segmented Regression Analysis

Drug	Effect	Rate Ratio	95% CI	P-value
Fluoroquinolones	Intervention*time	0.971	0.949–0.995	0.016
Ceftriaxone	Intervention*time	0.842	0.795–0.891	<0.001
Clindamycin	Intervention*time	0.931	0.904–0.958	<0.001

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1544. Impact of System-wide Adoption of CDC Core Elements on Antimicrobial Use and *Clostridium difficile* Infection in a Large Health System

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Background. Inappropriate Antimicrobial use, its associated resistance and suboptimal patient outcomes are important quality and safety concerns. Antimicrobial stewardship programs (ASP) can help reduce the risk of development of multi-drug resistant organisms, and Clostridium difficile infections. The Centers for Disease Control and Prevention (CDC) recommended core elements for successful implementation of ASPs in 2014. We describe the adoption of the core elements and associated outcomes at a large health system in the United States.

Methods. We organized our program based on the seven core elements. We focused on 1) making antimicrobial stewardship a system priority with full leadership support, 2) creating an infrastructure to promote and disseminate best practices, 3) standardizing indications for use of the different antimicrobial classes promoting most narrow-spectrum agents, and 4) building capacity for hospitals to achieve their goals from local leadership buy-in to infrastructure to do the work.

Results. Local ASPs were established in 89 hospitals. 3.3 million defined daily doses (DDDs) were used in FY15 compared with 2.9 million in FY16 and 2.8 million in FY 17. There was a drop in systemic antimicrobial use from 877 (FY15) to 809 (FY16) and 776 (FY17) DDDs/ 1000 patient-days ((7.7% and 4.1% reduction in FY 16 and FY 17; P <0.001) (Figure 1 and 2). In addition, hospital onset C. difficile lab ID events standardized infection ratios (SIR) dropped from 0.89 (events=2292) in FY15 to 0.84 (events=2056) in FY16 (5.6% reduction) and 0.75 in FY 17 (events=1818), a 10.7% reduction compared with FY16.

Conclusion. Implementation of the CDC core elements in a very large system has led to both an improvement in total systemic and targeted antibiotic use and reduction in C. difficile infections.