



Figure 3. ROC curves testing the patient-derived models in mice to differentiate strain 630g (low virulence/not severe) vs. VPI 10463 (high virulence/severe). The AUC and confidence interval for each model was the following: AUCs of 0.59 [0.44-0.74] (IDSA severity), 0.96 [0.90-1.0] (death), and 0.89 [0.81-0.97] (DRCs).

Disclosures. All Authors: No reported Disclosures.

77. Antimicrobial Prescribing Practices for Enteric Bacterial Infections in an Integrated Rural Healthcare System, 2004–2017

Scott C. Olson, MD¹; Louise Francois Watkins, MD, MPH²; Louise Francois Watkins, MD, MPH²; Elaine Scallan Walter, PhD³; Cindy R. Friedman, MD⁴; Cindy R. Friedman, MD⁴ and Huong McLean, PhD, MPH⁵; ¹Marshfield Clinic Research Institution, Marshfield, Wisconsin; ²Division of Foodborne, Waterborne, and Environmental Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; ³University of Colorado-Denver, Aurora, Colorado; ⁴CDC, Atlanta, Georgia; ⁵Marshfield Clinic Research Institute, Marshfield, Wisconsin

Session: 31. Not Just Your Everyday Diarrhea
Thursday, October 3, 2019: 10:42 AM

Background. Bacterial enteric infections are common in the United States, but few studies have evaluated antibiotic prescribing practices for these illnesses. Unnecessary antibiotics can lead to adverse events and emergence of antimicrobial resistance. We assessed treatment practices among patients with laboratory-confirmed enteric infections in a large regional healthcare system.

Methods. We used electronic health records to identify patients with laboratory-confirmed nontyphoidal *Salmonella*, *Shigella*, Shiga toxin-producing *E. coli* (STEC), and *Campylobacter* infections from 2004 to 2017. We extracted relevant clinical data, including diagnosis codes for chronic conditions and receipt of immunosuppressive medications in the 60 days before and after the encounter, and antibiotic prescriptions in the 14 days after the encounter. We defined an appropriate treatment based on pathogen, patient characteristics, and IDSA practice guidelines for the study period.

Results. We identified 2,064 patients infected with enteric pathogens: 1,251 (61%) with *Campylobacter*, 564 (27%) *Salmonella*, 199 (10%) STEC, and 50 (2%) *Shigella*. Overall, 425 (20%) patients were immunocompromised, ranging from 17% for *Salmonella* to 46% for STEC. There were 220 (11%) hospitalizations. The frequency of antibiotic prescribing was highest for *Campylobacter* (60%), followed by *Shigella* (50%) and *Salmonella* (49%). Prescriptions were appropriate for 62% of *Campylobacter* cases, 92% of *Shigella*, and 70% of *Salmonella*. Antibiotics were prescribed for 39% of STEC infections although they are generally not indicated. Appropriate treatment was highest for children with *Campylobacter* (87%) and lowest for adults ≥ 50 years with *Campylobacter* (42%). Among those with *Salmonella*, appropriate treatment was higher in those with a comorbidity (79% vs. 68% without, $P < 0.05$). Rates of appropriate use did not improve over time.

Conclusion. Antibiotic prescribing for laboratory-confirmed enteric infections was frequently inappropriate and inconsistent with practice guidelines. Antibiotic stewardship initiatives should address acute bacterial gastrointestinal infections in addition to other common infections.

Disclosures. All Authors: No reported Disclosures.

78. Oral Norovirus Vaccination in Humans Induces Plasmablast B-Cell Expansion and Follicular T-Cell Activation Comparable to Natural Infection

Roberto Mateo, PhD; Karen Lin, MS; Nikita Kolhatkar, PhD; David Taylor, MD; Shaily Garg, BS and Sean Tucker, PhD; Vaxart, Inc., San Francisco, California

Session: 31. Not Just Your Everyday Diarrhea
Thursday, October 3, 2019: 10:55 AM

Background. Norovirus (NoV) is a common cause of acute gastroenteritis, but no vaccines are currently licensed. Vaxart is developing an oral tableted NoV vaccine that induces both systemic and mucosal immune responses.

Methods. Two separate clinical studies were conducted to evaluate the safety and immunogenicity of an oral NoV vaccine and NoV infection. The first study investigated an oral tablet vaccine based on a recombinant adenovirus vector expressing NoV VP1 (rAd-VP1). In the second study, a controlled NoV infection (Norwalk virus) was performed using a strain isolated and purified from an infected subject. Serum and PBMCs were collected pre- and post-immunization/infection. Serum immune responses were assessed using IgG/IgA ELISAs and blocking titer (BT50) assays. Cellular immune responses were evaluated using antibody-secreting cell (ASC) assays to quantitate norovirus-specific B cells. Flow cytometry was used to analyze the phenotype of circulating B and T cells.

Results. The rAd-VP1 vaccine was well tolerated whereas most subjects (56%) in the controlled infection study had significant gastroenteritis 2–4 days post-inoculation. Subjects in cohorts vaccinated 28 days apart with 1×10^{10} or 1×10^{11} IUs showed the highest rises in serum IgG and IgA titers compared with those immunized 2 or 7 days apart with a 1×10^{10} IU vaccine dose. Subjects in the 1×10^{11} IU vaccine dose cohort had a 6-fold rise in serum IgA and 4-fold rise in BT50 titers, with mean IgA and IgG ASC values of 698 and 389 counts, respectively. In comparison, NoV-challenged subjects showed an average of 2,072 IgA and 886 IgG ASC counts. Remarkably, flow cytometry analysis revealed that activated B- and T-cell responses were similar post-vaccination and post-infection, with significant expansion of T follicular cells, plasmablasts, mucosal homing B cells, and preferential activation of IgA B cells.

Conclusion. The phenotype of activated B and T cells induced post-immunization was similar to that induced post-infection, suggesting that an oral vaccine can induce comparable adaptive immune responses without the substantial adverse clinical events that occur from natural infection. Future work in dose ranging will aid in the development of a safe and efficacious oral NoV vaccine.

Disclosures. All Authors: No reported Disclosures.

79. Mucosal Interferon (IFN) Responses in Infants with Respiratory Syncytial Virus (RSV) Infection to Inform Live Attenuated Vaccine (LAV) Development

Jeanette Taveras, DO¹; Cristina Garcia-Maurino, MD²; Sara Mertz, BS¹; Mark E. Peebles, PhD³; Octavio Ramilo, MD⁴; Octavio Ramilo, MD⁴ and Asuncion Mejias, MD, PhD, MSc¹; ¹Nationwide Children's Hospital, Grandview Heights, Ohio; ²Center for Vaccines and Immunity, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio; ³The Ohio State University, Columbus, Ohio; ⁴Nationwide Children's Hospital; and Ohio State University, Columbus, Ohio

Session: 31. Not Just Your Everyday Diarrhea
Thursday, October 3, 2019: 11:07 AM

Background. Respiratory syncytial virus (RSV) is a leading cause of hospitalization for infants. Several vaccine strategies for RSV are being developed. Among those, live attenuated vaccine (LAV) represent an attractive alternative for young children as they mimic natural infection and induce protective immunity without causing enhanced disease. However, markers of reactogenicity and/or innate immune protection in the respiratory mucosa are not well defined. The objective of this study was to assess mucosal markers, including innate immune cytokine profiles and RSV loads (VL), and their potential association with protection from severe disease in infants with natural RSV infection.

Methods. Single-center, prospective study in previously healthy infants with mild (outpatients; OP) and severe (inpatients; IP) RSV infection, and aged-matched healthy controls (HC). Nasopharyngeal (NP) swabs were obtained at enrollment in all subjects to measure VL by PCR, and cytokine concentrations (conc.) using a 13-plex panel that included: Type-I, type-II, and type-III IFN, and inflammatory cytokines. Cytokine conc. and VL were compared according to hospitalization status (OP vs. IP).

Results. From 2014 to 2017 we enrolled 105 infants: 48 with severe RSV infection (IP; median IQR age: 2.3 [1.1–5.5] months), 36 with mild disease (OP; 6.4 [3.8–9.3] months), and 20 HC (4.9 [2.8–7.2] months). The median duration of symptoms at enrollment was 4 days for both IP and OP. IL-1 β , TNF- α , and IL-10 were detected more frequently in RSV infants than in HC (39% vs. 5%, respectively), but median conc. in IP and OP were not different ($P > 0.05$). Detection and/or conc. of IFN- β , IP-10, IFN- γ and type III IFN (IFN- λ 1, IFN- λ 2/3) were significantly greater in OP vs. IP, who also had higher VL (Table 1). In addition, IP-10 ($r = 0.6$; $P < 0.001$) and IFN- λ conc. ($r = 0.55$, $P < 0.0001$) significantly correlated with RSV VL.

Conclusion. Infants with mild RSV infection had higher VL and a more robust type-I, -II, and -III IFN responses than those hospitalized with severe disease. These findings suggest that increase conc. of mucosal IFNs are associated with protection against severe RSV infection, and could potentially be used as surrogate markers to help the development of LAV for RSV infection in young children.