77. Antimicrobial Prescribing Practices for Enteric Bacterial Infections in an Integrated Rural Healthcare System, 2004–2017
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Session: 31. Not Just Your Everyday Diarrhea
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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 rural 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%) with Salmonella, 199 (10%) with STEC, and 50 (2%) with 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 highest 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
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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 adenosine 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-infection/serum. Serum immune responses were assessed using IgG/IgA ELISAs and blocking titer (BT30) assays. Cellular immune responses were evaluated using antibody-secretory cell (ASC) assays to quantitate norovirus-specific B cells.

Results. The rAd-VP1 vaccine was well tolerated whereas most subjects (50%) in the controlled infection study had significant gastroenteritis 2–4 days post-inoculation. Subjects in cohorts vaccinated 28 days apart with 1 x 10^11 or 1 x 10^13 RUS showed the highest rises in serum IgG and IgA titers compared with those immunized 2 or 7 days apart with a 1 x 10^11 IU vaccine dose. Subjects in the 1 x 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 counts 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, plasma blasts, mucosal homing B cells, and preferential activation of IgA B cells.

Conclusion. The phenotype of activated B and T cells induced post-infection was similar to that induced post-vaccination, 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 aide in the development of a safe and efficacious oral NoV vaccine.

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79. Mucosal Interferon (IFN) Responses in Infants with Respiratory Syncytial Virus (RSV) Infection to Inform Live Attenuated Vaccine (LAV) Development
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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 natural infection (LAV) represent an attractive alternative for young children to induce mucosal protection as it is capable of enhancing 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 (concs.) 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 115 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 OP and IP. IL-10, 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-λ1, IFN-λ2) 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 increases 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.

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80. Opioid Analgesics Are Associated With Increased Clostridioides difficile Infectious Risk in the Veteran Cohort of Years

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Session: 31. Not Just Your Everyday Diarrhea Thursday, October 3, 2019: 11:19 AM

Background. Clostridioides difficile infection (CDI) is the leading cause of healthcare-associated diarrhea. Several drugs are known to increase CDI risk, although the association between opioids and CDI risk has not been clearly established. Opioid analgesics have gastrointestinal antimotility and immunomodulatory effects, which may predispose patients to infection. The purpose of this study was to determine the association between opioid use and CDI risk.

Methods. This was a retrospective case-control study that utilized inpatient and outpatient data from the national United States Veterans Health Administration (VHA). CDI patients included those age 18 to 89 years with an ICD-9-CM code for CDI (008.45), a positive stool test, and active CDI therapy between October 1, 2002, and September 30, 2014. A control cohort of VHA patients was created by randomly sampling patients without a CDI ICD-9-CM code during the study period and matched to CDI patients by visit setting and fiscal year. Opioid use was defined as at least one prescription for morphine, hydromorphone, hydrocodone, and/or codeine in the 90 days prior to study inclusion. The χ² test was used to compare the proportion of patients who received an opioid in the CDI and control groups. Opioid risk factors for CDI were analyzed using a multivariable logistic regression model that included 33 covariates.

Results. A total of 85,451 patients were included in this study (26,149 CDI and 59,302 controls). Overall, 50.1% and 30.1% of patients were prescribed an opioid in the CDI and control group, respectively. Overall, opioids were associated with significantly increased CDI risk (OR 1.92, 95% CI 1.86–2.00) and was even greater for >1 opioid (OR 2.40, 95% CI 2.25–2.55). Opioids with the strongest association with CDI risk include morphine (OR 2.04, 95% CI 1.95–2.13), followed by hydromorphone (OR 1.74, 95% CI 1.63–1.87), codeine (OR 1.56, 95% CI 1.44–1.70), and hydrocodone (OR 1.14; 95% CI 1.09–1.19).

Conclusion. In a national cohort of veterans, patients with recent opioid analgesics use had an increased risk of developing CDI compared with a control group. Opioids with greater immunomodulatory and constipating effects were associated with increased risk compared with other opioids.

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81. Azithromycin-Nonsusceptible Salmonella New Port Infections Associated With Mexican-style Soft Cheese and Beef—The United States, 2018–2019

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

Background. Azithromycin is a recommended oral agent for treating non-typhoidal Salmonella (NTS), when antibiotics are indicated. Azithromycin nonsusceptibility among NTS is <1% in the United States. CDC, FSIS, and state health departments investigated an outbreak of azithromycin-nonsusceptible Salmonella serotype New Port infections to determine sources.

Methods. We classified isolates as the outbreak strain if they were within 11 alleles by core genome multilocus sequence typing. We defined a case as infection with the outbreak strain during June 2018–February 2019. After stratifying by gender and ethnicity, we compared food exposures ≤7 days before illness onset with those reported by healthy persons in the Foodborne Diseases Active Surveillance Network population survey (2006–2007). We used both multiclassification to determine antimicrobial susceptibility.

Results. We identified 218 case patients from 31 states; 49 of 176 (28%) were hospitalized and 2 died. Overall, 65% (121/187) were Hispanic, and 41% (70/169) visited Mexico in the 7 days before illness onset. Among travelers to Mexico, 71% (23/32) reported eating Mexican-style soft cheese; 1623 (70%) recalled obtaining the cheese in Mexico. Among nontravelers, the proportion who ate Mexican-style soft cheese (30%, 18/60) was similar to that reported by healthy persons, whereas the proportion who consumed beef (91%, 60/66) was higher than reported by healthy persons (P = 0.04). The outbreak strain was detected in a sample of soft cheese obtained in Mexico, and in a cecal sample from a steer and a beef sample that was collected at FSIS-regulated establishments in the United States. Isolates were resistant to ampicillin and trimethoprim–sulfamethoxazole, nonsusceptible to azithromycin, and showed decreased susceptibility to ciprofloxacin.

Conclusion. This is the first documented outbreak of azithromycin-nonsusceptible Salmonella infections in the United States. Two food vehicles—soft cheese obtained in Mexico, and beef obtained in the United States—were epidemiologically and genetically associated with this outbreak. Further investigation is warranted to determine the routes of entry, prevalence, and spread of azithromycin-nonsusceptible Salmonella in US and Mexican cattle.

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82. First 5 Years of Experience with the Illinois Extensively Drug-Resistant Organism (XDRO) Registry and Implementation of Automated Alerting

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Session: 32. Surveillance in Healthcare-associated Infections Thursday, October 3, 2019: 10:30 AM

Background. The Illinois XDRO Registry was created in November 2013 as an information system for XDROs; currently, the registry includes carbapenem-resistant Enterobacteriaceae (CRE), carbapenemase-producing Pseudomonas aeruginosa, and Candida auris. All Illinois healthcare facilities can manually query the registry at the time of admission to assess patients’ prior colonization status. A subset of facilities, mainly hospitals, participate in the registry’s automated querying process; alerts are automatically sent and via email, page, or text to infection preventionists at the time of patient admission.

Methods. We assessed counts of XDRO report submissions and total queries (manual and automated) over time, by organism. Facilities achieved automated alerts by sending a near-real-time feed of inpatient admission data (patient name and date of birth) to Illinois Department of Public Health (IDPH) via one of the three connection types: direct (data sent directly to IDPH), vendor (data sent via vendor software), and syndromic surveillance (existing syndromic surveillance data adapted for registry).

Results. In total, 6,445 unique patients (11,258 total reports) from 213 facilities have been reported to the XDRO registry (counts by organism type, Table). The registry has been manually queried 39,678 times by 232 facilities. Seventy-five facilities have queried the XDRO registry information system for XDROs; currently, the registry includes carbapenem-resistant Enterobacteriaceae, carbapenemase-producing Pseudomonas aeruginosa, and Candida auris. All Illinois healthcare facilities can manually query the registry at the time of admission to assess patients’ prior colonization status. A subset of facilities, mainly hospitals, participate in the registry’s automated querying process; alerts are automatically sent and via email, page, or text to infection preventionists at the time of patient admission.

Conclusion. The XDRO registry, originally focused on CRE, successfully expanded to include emerging XDRO threats such as Candida auris and is poised for rapid response to emerging threats. The registry’s adaptive querying structure and expanding automation have enabled it to deliver an increasing number of actionable infection-control alerts over time.

Table. Extensively Drug Resistant Organism Types Reported to XDRO Registry

| Organism | Date That First Case in Illinois | Date of First Report to XDRO Registry | Lag From Outbreak to Report in Months | Unique Patients (as of April 2019) |
|----------|---------------------------------|--------------------------------------|--------------------------------------|----------------------------------|
| Carbapenem-resistant Enterobacteriaceae | December 1, 2007 | November 2013 | 72 | 6,140 |
| Candida auris | May 2016 | January 2017 | 9 | 598 |
| Vancomycin-resistant Enterococci | November 2016 | April 2017 | 6 | 78 |