410. Influence of Pre-season Antibody Titers to Influenza Virus in Risk in a Cohort of Healthcare Personnel

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Background. Influenza (flu) and other respiratory viruses circulate regularly throughout healthcare systems, often placing healthcare personnel (HCP) at high risk for illness. Hemagglutination inhibition (HAI) titers are associated with protection from flu illness, though few studies have characterized HAI in HCP. The Respiratory Protection Effectiveness Clinical Trial (ResPECT), provided HAI titers and data to assess infection risk based on four flu seasons. Participants from multiple outpatient settings wore respiratory protection within six feet of symptomatic patients.

Methods. Serological samples obtained at the beginning and end of each season and anterior nasopharyngeal swabs were taken randomly and when patients reported respiratory symptoms were assessed. Our primary outcome was PCR-confirmed influenza.

Results. During 5,180 participant-seasons of observation, 128 PCR-confirmed influenza A infections (20 H1N1, 108 H3N2) and 34 PCR-confirmed influenza B infections. 4,041 (88%) reported receiving an annual influenza vaccine. Each log2-increase in titer subtype-specific titer reduced the hazard of influenza infection with A/ H3N2 by 18%(Relative Risk (RR) 0.82 95% CI 0.72,0.94), by 28% for influenza B (RR 0.72 95% CI 0.56,0.92 and by 25% for influenza A H1N1 (RR 0.75 95% CI 0.57–1.0). After adjusting for HAI titers, age was not significantly associated with risk for any of the subtypes.

Conclusion. In this prospective cohort of monitored HCPs, these findings support the current literature demonstrating that HAI titers are associated with protection from influenza infection. The relationship between HAI titers, influenza, and vaccination is complex, however. Vaccination was not shown to be associated with infection risk or protective effect.

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411. Does an Early Cytokine Response During Ebola Virus Disease Improve the Duration of Survival in Rhesus Macaques?

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Background. Ebola virus disease results in a severe cytokine release resulting in organ failure and disseminated intravascular coagulation, often leading to death. An early post-exposure immune response may improve outcomes but that remains poorly characterized. Therefore, we evaluated select serum cytokine markers of immune activation in nonhuman primates (NHPs) for their association with duration of survival.

Methods. This was a post-hoc analysis of an interventional supportive care NHP study in which 13 rhesus macaques were inoculated intramuscularly with a target dose of 1000 PFU Zaire ebolavirus (Kikwit). We measured cytokines with a Luminex MAGPIX panel at baseline and daily starting day 3 post-exposure until euthanasia.

Based on human clinical data, 10 cytokines and proteins were included in our analysis: IL-1β, IL-6, IL-10, GM-CSF, MCP-1, MIP-1α, MIP-1β, IFN-γ, TNF-α, and C-reactive protein. After NHPs were divided into two groups by k-means clustering, we developed Kaplan-Meier curves for time to death (Figure 1). We visually explored Pearson’s correlation and kinetics of serum cytokines and log10-viral load (Figure 2). We fitted cox regression models with each cytokine to evaluate the risk of early death for each cytokine log10 level or log-fold change. We performed a sensitivity analysis for MIP-1β centering the data at dpe 0.

Results. Among NHPs with temperature data, 83%(N = 10) developed fevers (>3 SD baseline) from dpe 3 to 4. The macrophage marker MIP-1β was associated with an increased risk of early death (per logpg/mL increase, HR=5.28 at dpe 3, adjusted P = 0.045). Surprisingly, this association was also observed at dpe 0 (HR=3.68 at dpe 0, adjusted P = 0.044). Other cytokine levels or changes were not associated with an increased hazard of death.

Conclusion. Our findings did not support a role for early systemic cytokine release in improving survival. However, elevated baseline levels of the MIP-1β may predispose NHPs to early death from EVD. This finding could represent a target for therapeutic strategies and should be further researched.

Disclosures. All authors: No reported disclosures.

412. Host Response Biomarkers Predict Clinical Failure in Patients with Staphylococcus aureus Bacteremia (SAB) Treated with Fluoxacillin (FLU) or Vancomycin (VAN)

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Background. Imbalance among innate mediators such as IL-1β, IL-10, and TNFα portends poor outcomes of persistence and death in patients with SAB. Previous studies did not consider the role of antibiotic treatment in this important host–pathogen relationship. In this study of SAB, we determined cytokine signatures that correlate with the composite endpoint of clinical failure (bacteremia duration >4 days or 30-day mortality) in Australian patients treated with FLU or VAN.

Methods. Sera from 86 patients with SAB (24.4% MRS) were obtained from a clinical study of patients treated with FLU or VAN. All of the patient samples were collected at clinical presentation (day 0 or day 1 of infection) and were treated with FLU or VAN throughout. Patients were classified into either clinical success (CS = 68) or clinical failure (CF = 18), defined as death or prolonged bacteremia >4 days. Patient