LB18. Understanding Zika-Specific Immunity for Prevention and Protection

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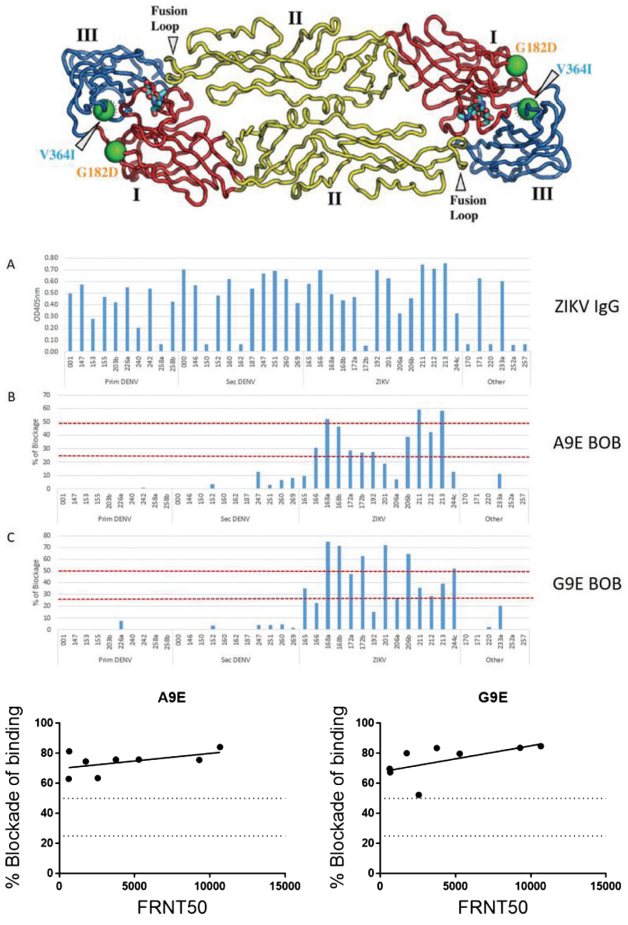
Background. Flavivirus infection represents a major public health problem, with over 2 billion people at risk for one or more infections each year. There are no licensed antiviral treatments for flaviviruses, and effective vaccines are lacking for several. Accurate diagnosis of flaviviruses is also complicated by serologic cross-reactivity. Thus, there is an urgent need to develop public health tools and interventions to reduce the burden of flavivirus infection worldwide.

Methods. We recently isolated two potently neutralizing human monoclonal antibodies (NmAb) against Zika, which exhibit activity against multiple strains of Zika but do not bind the closely related dengue virus. Mapping studies revealed that the NmAb target distinct epitopes on the envelope protein (E). A competition ELISA (ZE-BOB) was developed with the two NmAb to test the hypotheses that neutralizing Ab responses in the general population would target the same epitopes on Zika E as the novel NmAb.

Results. We found that competitive Ab responses were detected in 19 of 19 (100%) convalescent sera from travelers with confirmed Zika infection. We tested a panel of 20 sera from individuals with either primary or secondary prior dengue infection and found that 18/20 (90%) contained IgG reactive with Zika virus; however, 0/20 (0%) exhibited ZE-BOB activity. These results indicate that the epitopes targeted by these two Zika NmAb are consistently immunogenic humans infected by Zika. Additionally, these epitopes elicit type-specific Ab to Zika, providing a basis for development of simple serodiagnostic assays with utility in epidemiologic studies as well as in the clinical setting. Because NAb are key determinants of long-term protection against future flavivirus infection, we further hypothesized that the results of the ZE-BOB assay may simultaneously provide a correlate of immunity, which would be a critical tool for vaccine development. In comparing the 50% neutralization titer against Zika with the magnitude of competition by ZE-BOB, there was no correlation in these values, but sera tended to be positive in both or neither assay.

Conclusion. Therefore, the ZE-BOB assay constitutes a novel tool that is widely deployable for purposes ranging from clinical diagnosis to epidemiologic monitoring to vaccine development for Zika.



Disclosures. All authors: No reported disclosures.

LB19. Patterns of Influenza A Hospitalizations by Subtype and Age in the United States, FluSurv-NET, 2018–2019

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Background. The 2018–19 influenza season was characterized by prolonged co-circulation of Influenza A H3N2 (H3) and H1N1pdm09 (H1) viruses. We used data from the Influenza Hospitalization Surveillance Network (FluSurv-NET) to describe age-related differences in the distribution of influenza A subtypes.

Methods. We included all cases residing within a FluSurv-NET catchment area and hospitalized with laboratory-confirmed influenza during October 1, 2018–April 30, 2019. We multiply imputed influenza A subtype for 63% of cases with unknown subtype and based imputation on factors that could be associated with missing subtype including surveillance site, 10-year age groups and month of hospital admission. We calculated influenza hospitalization rates and 95% confidence intervals (95% CI) by type and subtype per 100,000 population. We compared the proportion of cases with H1 by year of age in FluSurv-NET to the distribution obtained from US public health laboratories participating in virologic surveillance and providing specimen-level influenza Results.

Results. Based on available data, 18,669 hospitalizations were reported; 41% received influenza vaccination ≥2 weeks prior to hospitalization and 90% received antivirals. Cumulative hospitalization rates per 100,000 population were as follows: H1 32.5 (95% CI 31.7–33.3), H3 29.3 (95% CI 28.5–30.1) and B 2.5 (95% CI 2.3–2.7). Based on weekly rates, H1 hospitalizations peaked during February (week 8) and H3 hospitalizations during March (week 11) (Figure A). FluSurv-NET data showed distinct patterns of subtype distribution by age, with H1 predominating among cases 0–9 and 24–70 years, and H3 predominating among cases 10–23 and ≥71 years. Data on the proportion of H1 results by age correlated well between FluSurv-NET and US virologic surveillance (Figure B).

Conclusion. Influenza A H1 and H3 virus circulation patterns varied by age group during the 2018–2019 season. The proportion of cases with H1 relative to H3 was low among those born between 1996 and 2009 and those born before 1948. These findings may indicate protection against H1 viruses in age groups with exposure to H1N1pdm09 during the 2009 pandemic or to older antigenically similar H1N1 viruses as young children.

Figure A. Weekly Hospitalization Rates by Influenza Type/Subtype, FluSurv-NET, 2018-19 Influenza Season

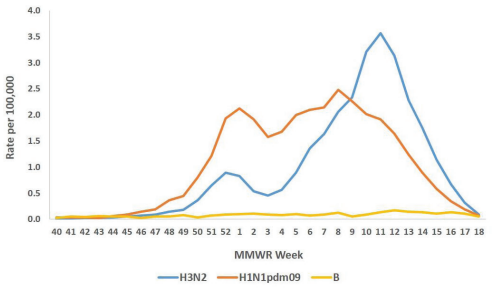
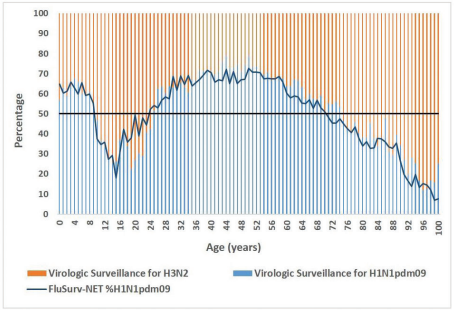


Figure B. Percentage of Persons with Influenza A H1N1pdm09 versus H3N2 by Age in FluSurv-NET and U.S. Virologic Surveillance, 2018-19 Influenza Season



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LB20. Valacyclovir to Prevent Vertical Transmission of Cytomegalovirus After Maternal Primary Infection During Pregnancy

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Background. Cytomegalovirus (CMV) is the most common cause of congenital infection in humans. The highest risk of fetal injury follows a maternal primary infection early in pregnancy. Despite the potential for severe fetal injury, to date there are no proven means to prevent viral transmission. Valacyclovir is an antiviral drug proven effective in decreasing the risk for CMV infection among transplant recipients. Valacyclovir is safe for use in pregnancy, and concentrates in the amniotic fluid without accumulating. A dose of 8 g/day creates therapeutic drug levels in the amniotic fluid and fetal blood.

Methods. This is a randomized, double-blind, placebo-controlled study comprising pregnant women with serologic evidence of primary CMV infection during the periconceptional period and first trimester. After informed consent, patients were randomly assigned to a treatment group (8 g/day of Valacyclovir) or control group (placebo). Treatment was initiated at the time of serological detection, and continued until amniocentesis. The primary endpoint was the rate of vertical transmission of CMV—determined by amniotic fluid CMV PCR. Secondary endpoints included evidence of symptomatic congenital CMV infection—in utero or postnatally.

Results. ***One hundred*** women were recruited, 90 were included in the data analysis; 45 patients received Valacyclovir and 45 placebo. There were 2 twin pregnancies, and therefore 92 amniocentesis. Amongst the Valacyclovir group, 5 (11.1%) amniocentesis were positive for CMV, compared with 14 (29.8%) in the placebo group (P GLMM = 0.03), corresponding with an odds ratio of 0.29 (95% CI: 0.09–0.90) for vertical CMV transmission. Amongst patients infected during the first trimester, a positive amniocentesis for CMV was significantly ($P = 0.02$) less likely in the Valacyclovir arm (2/19) compared with placebo (11/23). No significant differences ($P = 0.91$) in CMV-positive amniocentesis were observed between study arms amongst patients infected periconceptionally.

Conclusion. Valacyclovir at a dose of 8 g/day is effective in reducing the rate of fetal CMV infection following early maternal primary infection during pregnancy. The drug reduces the rate of fetal infection by 71%.

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

LB21. The Seattle Flu Study: A Community-Based Study of Influenza

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Background. Influenza epidemics and pandemics cause significant morbidity and mortality. An effective response to a potential pandemic requires the infrastructure to rapidly detect and contain new and emerging flu strains at a population level. The objective of this study was to use data gathered simultaneously from community and hospital sites to develop a model of how flu enters and spreads in a population.

Methods. In the 2018–2019 season, we enrolled individuals with respiratory illness from community sites throughout the Seattle area, including homeless shelters, childcare facilities, Seattle-Tacoma International Airport, workplaces, college campuses, clinics, and at home (Figure 1). We collected data and nasal swabs from individuals with at least two respiratory symptoms. Additionally, we collected residual nasal swabs and data from individuals who sought care at four regional hospitals. Home-based self-testing for influenza and prediction models for influenza were piloted. Swabs were tested with a multiplex molecular assay, and influenza whole-genome sequencing was performed. Geospatial mapping and computational modeling platforms were developed to characterize regional spread of respiratory pathogens.

Results. A total of 18,847 samples were collected in the 2018–2019 season. Of those tested to date, 291/3,653 (8%) community and 2,393/11,273 (21%) hospital samples have influenza detected. Of the community enrollments, 39% had influenza-like illness. Community enrollees were in age groups not well-represented from hospitals. Influenza A/H3N2 activity peaked on college campuses and homeless shelters 2 weeks before the peak in hospitals. We observed multiple independent introductions of influenza strains into the city and evidence of sustained transmission chains within the city (Figures 2 and 3).

Conclusion. Utilizing the city-wide infrastructure we developed, we observed the introduction of influenza A/H3N2 into the community before the hospital and evidence of transmissions of unique strains into and within the Seattle area. These data provide the blueprint for implementing city-wide, community-based surveillance systems for rapid detection, real-time assessment of transmission patterns, and interruption of spread of seasonal or pandemic strains.

Figure 1. Targeted community enrollment sites in the Seattle region. The size of the circle represents the total number of enrollments at each site.

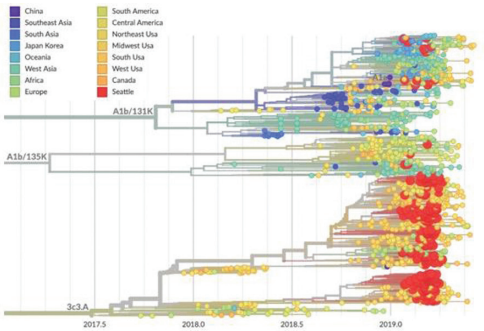

Figure 2. Phylogenetic tree of influenza A/H3N2, including 280 Seattle Flu samples (red dots) compared to strains observed globally.

Fig 3. Transmission chains of influenza A/H3N2 within Seattle, as well as introductions of strains that do not show signals of sustained transmission.

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