

2750. Sequential Influenza A H1N1 and Influenza A H3N2 Challenge Infections in Healthy Volunteers

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Background: Seasonal influenza causes significant annual morbidity and mortality. The effects of yearly exposures on immunity are not clear and recent observations have demonstrated that long lasting protection against a matched strain may not naturally occur. The 2018–2019 influenza season consisted of an initial peak of H1N1 infections followed by a wave of H3N2 infections. These consecutive waves raise questions about how influenza immunity is affected by sequential exposure to different influenza strains. Challenge studies provide a unique opportunity to study this phenomenon. Here we describe a subset of participants who were sequentially infected in two separate challenge studies with wild-type H1N1 and H3N2 viruses.

Methods: Healthy volunteers completed two sequential influenza challenge studies at the NIH Clinical Center. Participants were inoculated with reverse genetics, cell-based, GMP wild-type influenza viruses, A(H1N1)pdm09 and A(H3N2) strains. Participants remained isolated in the hospital for a minimum of 9 days and were monitored daily for viral shedding and clinical symptoms. After discharge, participants were followed for 2 months.

Results: Between 2014 and 2017, 14 healthy volunteers were exposed to Influenza A(H1N1) and Influenza A(H3N2). Time between infections ranged from 2 months to 2 years. Thirteen (93%) participants developed confirmed influenza infection after H1N1 challenge and 9 (64%) after H3N2 challenge. Eight (57%) participants developed confirmed infections after both exposures. Variable degrees of symptoms, shedding, and disease severity were observed. Systemic antibody responses to the HA and NA of both H1N1 and H3N2 varied over time during these sequential infections.

Conclusion: More than half of all participants who completed 2 sequential H1N1 and H3N2 challenge studies demonstrated confirmed infection to both viruses. These sequential infections had varying effects on the disease experienced and the immunity that developed after infection. These observations are important in understanding the impact of sequential exposures on influenza immunity.

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2751. Pragmatic Assessment of Influenza Vaccine Effectiveness in the DoD (PAIVED): Methods

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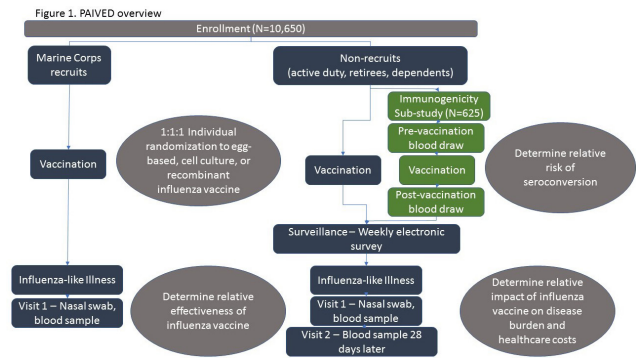
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Background: Most influenza vaccines come from inactivated virus grown in egg culture, and studies suggest that egg-adapted virus may have decreased immunogenicity in humans for certain influenza A strains. Cell culture-based and recombinant vaccines may be more immunogenic, but comparative studies are lacking. We are conducting a randomized, controlled trial of 3 FDA-licensed influenza vaccines (cell culture, recombinant, and egg culture) to assess differences in immunogenicity and effectiveness in adults.

Methods: A total of 10,650 eligible adults will be individually randomized 1:1:1 (cell culture, recombinant, or egg-based vaccine) over 2 influenza seasons (2018–2019 and 2019–2020) at military facilities in geographically diverse locations in the US. Participants who are not military recruits will report the presence or absence of ILI symptoms on a weekly basis through an automated electronic (text message or email) survey; those who experience ILI symptoms will be scheduled for two in-person visits. Military recruits who experience an ILI report will report directly to clinic and will not receive weekly surveillance reminders (Figure 1).

Results: Enrollment for year 1 of PAIVED occurred November 7 to December 31, 2018 at 5 military bases. During this season, 1,623 participants were enrolled, among whom 34% were randomized to receive cell culture vaccine, 33% to recombinant vaccine, and 33% to egg-based vaccine. The participants were 61% active military, 19% retired military, and 20% military dependents. One quarter of the participants were women, and the participants were 18–88 years old, median 26 years of age. Among the 1,559 participants with complete data, 324 (21%) experienced ILI at least once. Blood and swab samples were successfully collected at visit 1 from 93% of the participants with case-defined ILIs.

Conclusion: The initial phase of PAIVED successfully enrolled and randomized 1,623 participants during the 2018/2019 influenza season. Follow-up of this season's participants is on-going. PAIVED will apply lessons learned during the 2018/2019 influenza season to the next season's study implementation, with the goal of enrolling more than 9,000 additional participants through increasing the number of individuals enrolled at some sites and adding new sites to the trial.



Disclaimer

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The investigators have adhered to the policies for protection of human subjects as prescribed in 45CFR46.

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2752. Peptide Vaccines Utilizing Conserved Hemagglutinin, Neuraminidase, and Matrix Ectodomain Influenza Epitopes Demonstrate Functional Activity Against Group 1 and 2 Influenza Strains

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