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Vaccine preventable disability: the vitality path to discovering effective vaccines for older adults

Janet E. McElhaney
Health Sciences North Research Institute, Northern Ontario School of Medicine, Canada

Statement of the Problem: Influenza illness in older adults leads to as many as 810,000 hospitalizations per year in the US. We have shown that nearly one-fifth of older adults will experience catastrophic outcomes following hospitalization including disability (10%) or death (8%). These outcomes should be preventable by influenza vaccination but vaccine effectiveness is low in older adults. Our approach to improving influenza vaccines for older adults seeks to overcome two obstacles. First, we need to know specifically why frail older adults fail to respond, because as we have shown, it is frailty rather than mere chronological that age limits vaccine effectiveness – but older adults are commonly excluded from influenza vaccine research. Second, cell-mediated immune (CMI) responses are understudied as measures of immune protection in older adults, but are crucial for vaccine effectiveness. Methodology: Older adults reflecting the spectrum of frailty in the over 65 population are recruited for our vaccination studies. We use our well-established ex vivo influenza A/H3N2 challenge model in peripheral blood mononuclear cells (PBMC) to simulate the response to natural influenza infection. Correlates of vaccine effectiveness have been established using biologic activity assays of the cytolytic mediator, granzyme B (GrB), in ex vivo PBMC lysates and interferon-□ (IFN□□ and interleukin-10 (IL-10). Split-virus influenza vaccines (SVV) only weakly stimulate IFN□ and GrB independent of vaccine dose. In contrast, high dose (HD) vs. standard dose (SD) SVV stimulates higher levels of IL-10 and corresponds to the enhanced antibody response to HD-SVV. IL-10 suppresses the inflammatory response to influenza vaccination that suppresses the formation of T follicular helper cells necessary for antibody production. Conclusion & Significance: the benefit of HD over SD SVV in older adults may be largely antibody-mediated but not necessarily limited to the neutralizing effects measured in hemagglutination inhibition assays.

Biography

Janet E. McElhaney, MD, FRCPC, FACP, is Scientific Director, Health Sciences North Research Institute, Professor of Medicine, Northern Ontario School of Medicine and holds the HSN Chair in Healthy Aging. The Vaccine Initiative To Add Life to Years (VITALiTY) focuses on the effect of aging and frailty on immune responses to influenza infection and vaccination, and how new vaccines can be designed to better protect older adults against the serious complications of influenza. The translation of this research is the development of immunologic correlates of vaccine effectiveness in older adults that can be used to advance new influenza vaccines or geroscience-guided interventions through the clinical development pipeline. She received the 2020 Jonas Salk Award from the March of Dimes Canada. Her research has been funded by the Canadian Institutes of Health Research, Public Health Agency of Canada, and NIH National Institute of Allergy and Infectious Diseases and National Institute of Aging.

jmcelhaney@hsnri.ca