## Transcript Details

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Immune Imprinting and Vaccines: Rethinking the First Exposure to Influenza

**Announcer:**
You're listening to ReachMD. This medical industry feature, titled "Immune Imprinting and Vaccines: Rethinking the First Exposure to Influenza," is sponsored by CSL Seqirus.

**Narrator:**
Our first flu is forever—but what does that really mean?

Immune imprinting refers to how the immune system's first encounter with a virus, such as influenza, leaves a lasting imprint that shapes future immune responses.[1,2] After the first viral exposure, subsequent encounters with viral variants prompt the immune system to primarily produce antibodies against the initial virus as well as neutralizing antibodies for the new viral variant.[1-4]

This can lead to the immune response being biased towards previously encountered antigens.[1,3] Take the real-world example of the H1N1 influenza pandemics. During a typical influenza season, elderly people are usually among the most vulnerable, with high rates of morbidity and mortality.[5,6] But during the H1N1 pandemic, the trend flipped, and many elderly people were better protected.[6]

This is likely because they were first exposed to a strain of H1N1 as infants during or after the 1918 pandemic, when the H1N1 virus was circulating.[4,6] That early exposure may have given their immune systems a lasting edge decades later. So for these patients, immune imprinting was biologically advantageous but influenza vaccines may affect this process—particularly when egg-based vaccines are used.[12]

While effective, traditional egg-based vaccines can inadvertently introduce antigenic mismatch due to egg adaptations.[7] This occurs when the virus mutates to replicate more efficiently within the eggs used for vaccine production.[7-11] These unpredictable changes can reduce seasonal vaccine effectiveness for everyone but immune imprinting amplifies this problem in children.[9-12]

One study found that infants whose first influenza exposure was to an *egg-adapted* vaccine produced a stronger antibody response to egg-propagated viruses than to viruses matching the circulating strain. However, infants who were first exposed through natural influenza infection and later received an egg-adapted vaccine showed a strong immune response to both egg-propagated and circulating viruses.[12] These findings suggest that immune imprinting may be influenced by adaptations introduced during egg-based vaccine development.

So, if an infant's first influenza exposure is to an egg-adapted vaccine this could cause the immune system to be biased towards mismatched antigens, potentially reducing protection against circulating strains for years to come.[11,12] Emerging evidence also shows that non-egg-based vaccines, such as cell-based influenza vaccines, avoid the risk of egg adaptation, which may provide better-matched antigens that may lead to stronger, more targeted immune responses.[8,11] And switching to non-egg-based vaccines, such as cell-based influenza vaccines, even across multiple seasons, could help redirect immune responses and could also create more effective defenses against circulating influenza strains in people of all ages.[11,12]

But for infants, the impact of receiving a non-egg-based vaccine for their first influenza vaccination may be even more profound potentially improving their immune response to circulating viruses both for the season as well as throughout their lifetime.[1,2] So, by understanding how vaccine types affect immune imprinting, we can harness its benefits and provide informed recommendations for our

patients and their families making sure their first flu exposure leaves a lasting, positive impact on their immunity.[12]

**Announcer:**
This program was sponsored by CSL Seqirus. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

**References:**

1. King SM, Bryan SP, Hilchey SP, Wang J, Zand MS. First impressions matter: Immune imprinting and antibody cross-reactivity in influenza and SARS-CoV-2. *Pathogens*. 2023;12(2):169. doi:10.3390/pathogens12020169
2. Zhang A, Stacey HD, Mullarkey CE, Miller MS. Original antigenic sin: How first exposure shapes lifelong anti-influenza virus immune responses. *J Immunol*. 2019;202(2):335–340. doi:10.4049/jimmunol.1801149
3. Kelvin AA, Zambon M. Influenza imprinting in childhood and the influence on vaccine response later in life. *Euro Surveill*. 2019;24(48):1900720. doi:10.2807/1560-7917.ES.2019.24.48.1900720
4. Butler D. The ghost of influenza past. *Nature*. 2018;560:158–160.
5. Rolfes MA, Foppa IM, Garg S, et al. Annual estimates of the burden of seasonal influenza in the United States: A tool for strengthening influenza surveillance and preparedness. *Influenza Other Respir Viruses*. 2018;12(1):132–137. doi:10.1111/irv.12486
6. 2009 H1N1 Early Outbreak and Disease Characteristics. CDC. Updated October 27, 2009. Accessed April 9, 2025, https://archive.cdc.gov/www_cdc_gov/h1n1flu/surveillanceqa.htm
7. Peck H, Laurie KL, Rockman S, et al. Enhanced isolation of influenza viruses in qualified cells improves the probability of well-matched vaccines. *NPJ Vaccines*. 2021;6(1):149. doi:10.1038/s41541-021-00415-3
8. How influenza (flu) vaccines are made. CDC. Updated November 3, 2022. Accessed November 13, 2024. https://www.cdc.gov/flu/vaccine-process/index.html
9. How flu viruses can change: “drift” and “shift”. CDC. Updated September 17, 2024. Accessed November 12, 2024. https://www.cdc.gov/flu/php/viruses/change.html
10. Paules CI, Sullivan SG, Subbarao K, Fauci AS. Chasing seasonal influenza - The need for a universal influenza vaccine. *N Engl J Med*. 2018;378(1):7–9. doi:10.1056/NEJMp1714916
11. Rockman S, Laurie K, Ong C, et al. Cell-based manufacturing technology increases antigenic match of influenza vaccine and results in improved effectiveness. *Vaccines (Basel)*. 2022;11(1):52. doi:10.3390/vaccines11010052
12. Liu F, Gross FL, Jefferson SN, et al. Age-specific effects of vaccine egg adaptation and immune priming on A(H3N2) antibody responses following influenza vaccination. *J Clin Invest*. 2021;131(8):e146138. doi:10.1172/JCI146138

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