I BEST OF THE WEEK (15 ago – 19 ago 2022)

R. Link-Gelles et al.

Effectiveness of 2, 3, and 4 covid-19 mrna vaccine doses among immunocompetent adults during periods when sars-cov-2 omicron ba.1 and ba.2/ba.2.12.1 sublineages predominated — vision Network, 10 States, December 2021–June 2022

MMWR Morb Mortal Wkly Rep, July 2022; doi: 10.15585/mmwr.mm7129e1

Abstract

The Omicron variant (B.1.1.529) of SARS-CoV-2, the virus that causes COVID-19, was first identified in the United States in November 2021, with the BA.1 sublineage (including BA.1.1) causing the largest surge in COVID-19 cases to date. Omicron sublineages BA.2 and BA.2.12.1 emerged later and by late April 2022, accounted for most cases. Estimates of COVID-19 vaccine effectiveness (VE) can be reduced by newly emerging variants or sublineages that evade vaccine-induced immunity, protection from previous SARS-CoV-2 infection in unvaccinated persons, or increasing time since vaccination. Real-world data comparing VE during the periods when the BA.1 and BA.2/BA.2.12.1 predominated (BA.1 period and BA.2/BA.2.12.1 period, respectively) are limited. The VISION network examined 214,487 emergency department/urgent care (ED/UC) visits and 58,782 hospitalizations with a COVID-19-like illness diagnosis among 10 states during December 18, 2021-June 10, 2022, to evaluate VE of 2, 3, and 4 doses of mRNA COVID-19 vaccines (BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna]) compared with no vaccination among adults without immunocompromising conditions. VE against COVID-19-associated hospitalization 7-119 days and ≥120 days after receipt of dose 3 was 92% (95% CI = 91%-93%) and 85% (95% CI = 81%-89%), respectively, during the BA.1 period, compared with 69% (95% CI = 58%-76%) and 52% (95% CI = 44%-59%), respectively, during the BA.2/BA.2.12.1 period. Patterns were similar for ED/UC encounters. Among adults aged ≥50 years, VE against COVID-19-associated hospitalization ≥120 days after receipt of dose 3 was 55% (95% CI = 46%-62%) and ≥7 days (median = 27 days) after a fourth dose was 80% (95% CI = 71%-85%) during BA.2/BA.2.12.1 predominance. Immunocompetent persons should receive recommended COVID-19 booster doses to prevent moderate to severe COVID-19, including a first booster dose for all eligible persons and second booster dose for adults aged ≥50 years at least 4 months after an initial booster dose. Booster doses should be obtained immediately when persons become eligible.

L.B. Hartwell et al.

Intranasal vaccination with lipid-conjugated immunogens promotes antigen transmucosal uptake to drive mucosal and systemic immunity

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Abstract

To combat the HIV epidemic and emerging threats such as SARS-CoV-2, immunization strategies are needed that elicit protection at mucosal portals of pathogen entry. Immunization directly through airway surfaces is effective in driving mucosal immunity, but poor vaccine uptake across

the mucus and epithelial lining is a limitation. The major blood protein albumin is constitutively transcytosed bidirectionally across the airway epithelium through interactions with neonatal Fc receptors (FcRn). Exploiting this biology, here, we demonstrate a strategy of "albumin hitchhiking" to promote mucosal immunity using an intranasal vaccine consisting of protein immunogens modified with an amphiphilic albumin-binding polymer-lipid tail, forming amph-proteins. Amph-proteins persisted in the nasal mucosa of mice and nonhuman primates and exhibited increased uptake into the tissue in an FcRn-dependent manner, leading to enhanced germinal center responses in nasal-associated lymphoid tissue. Intranasal immunization with amph-conjugated HIV Env gp120 or SARS-CoV-2 receptor binding domain (RBD) proteins elicited 100- to 1000-fold higher antigen-specific IgG and IgA titers in the serum, upper and lower respiratory mucosa, and distal genitourinary mucosae of mice compared to unmodified protein. Amph-RBD immunization induced high titers of SARS-CoV-2-neutralizing antibodies in serum, nasal washes, and bronchoalveolar lavage. Furthermore, intranasal amph-protein immunization in rhesus macaques elicited 10-fold higher antigen-specific IgG and IgA responses in the serum and nasal mucosa compared to unmodified protein, supporting the translational potential of this approach. These results suggest that using amph-protein vaccines to deliver antigen across mucosal epithelia is a promising strategy to promote mucosal immunity against HIV, SARS-CoV-2, and other infectious diseases.