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Multi-Dose Vaccines Administered in the Same Site Boost Immune Response

New research suggests that receiving multiple doses of a vaccine in the same limb leads to faster antibody development, an important strategy for providing immunity as quickly as possible during a pandemic or disease outbreak.

The study, published in *The Journal of Immunology*, found that mice that received both doses of the COVID-19 vaccine in the same limb (ipsilateral) had a faster initial antibody response in the weeks after vaccination compared to those whose vaccines were administered in different limbs (contralateral). In the long term, both vaccination approaches resulted in similar antibody development or immunity levels.

Dr. Jennifer Juno, co-lead author from The Peter Doherty Institute for Infection and Immunity at the University of Melbourne said, "Our findings suggest that during disease outbreaks when rapid immune protection is crucial, healthcare providers may want to consider administering multiple vaccine doses in the same arm. This could help people develop protective antibodies more quickly, which is particularly important during active outbreaks or pandemics."

Dr. Hyon-Xhi Tan, co-lead author also from The Peter Doherty Institute for Infection and Immunity at the University of Melbourne, added, "This knowledge could inform vaccination strategies not just for COVID-19, but for other vaccines that require multiple doses. The findings provide valuable insights into how the immune system responds to vaccines in different locations, aiding in the development of more effective vaccination protocols."

Vaccine-specific immune responses begin in the lymph nodes closest to the vaccination site. Most adult and adolescent vaccinations are administered intramuscularly in the upper arm, with people choosing to be vaccinated in their non-dominant arm. The researchers wanted to understand the impact of administering subsequent doses of vaccines to either the same or different lymph nodes depending on the arm chosen, as these findings could optimize vaccine schedules and maximize immunity.

Due to the challenges of directly sampling human lymphoid tissues to assess antibody development, the research team utilized a mouse model. Mice were given two doses of the COVID-19 vaccine fourteen days apart, either twice on the left hind leg or once on the left hind leg and once on the right forearm. Immune responses were assessed at 19 and 28 days from vaccination.

In addition to finding that both doses of vaccine in the same location led to a faster initial antibody response, the researchers also discovered that when using vaccines designed for different COVID-19 variants, the choice of injection site influenced how immune cells in the lymph nodes responded

to the vaccines. A greater breadth of initial antibodies was produced when vaccinated with SARS-CoV-2 variants in the same limb. This indicates that an ipsilateral vaccination strategy could also be relevant in outbreak responses as viruses evolve or mutate. However, neither of these findings had an impact on long-term immunity.

The research team plans to investigate further the biological mechanisms behind the faster immune response from same arm vaccination. “We also want to determine if these findings extend to other vaccines, explore how the timing between doses affects location-based immune responses, and if other vaccine sites such as the lung impact this effect. This work could lead to more effective vaccination protocols across multiple diseases," said Dr. Tan.

The research article is available on *The Journal of Immunology* website.

Requests for interviews with authors, *The Journal of Immunology* or the American Association of Immunologists can be made to kpalmer@aai.org.

About The American Association of Immunologists
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