VACCIREVIEW

The lasting lessons of mpox: infection, vaccination, and immune memory

Bibliography

Mitjà O, Marks M. The lasting lessons of mpox: infection, vaccination, and immune memory. Lancet Infect Dis. 2026;26(2):118-119. doi:10.1016/S1473-3099(25)00596-1

Summary

This commentary reviews a 2-year cohort of 250 adults with orthopoxvirus exposure (natural mpox infection vs MVA-BN vaccination) and distils practical lessons on durability and quality of immune memory. Natural mpox infection induced robust neutralizing antibodies that remained detectable for up to 2 years, whereas individuals vaccinated with MVA-BN—especially those born after cessation of smallpox vaccination in the 1970s—showed weak and rapidly waning functional antibody responses, with neutralizing antibodies detectable in only a small minority beyond 8 months. People who had received historic, replication-competent smallpox vaccines (e.g. Dryvax) and were later vaccinated with MVA-BN had antibody titers similar to convalescent mpox cases, underlining the long-term imprinting by live-replicating vaccinia vaccines.

For practicing clinicians, the key message is that current third-generation MVA-BN vaccines are very safe, including in immunocompromised patients, but probably provide shorter-lived functional protection than natural infection or older smallpox vaccines. Subcutaneous administration at full dose elicited higher binding and neutralizing antibody titers than fractional intradermal dosing, arguing for standard-dose subcutaneous schedules in smallpox-naïve individuals whenever supply allows. The authors emphasize that next-generation mpox/smallpox vaccines will need to balance safety with more durable neutralizing responses, likely by focusing on key MPXV antigens such as E8 and A35 and optimizing antigen dose and delivery.

*Brought to you by Chief Editor **Joe Schmitt** – Supported by AI*