Swedish study indicates decline of neutralizing antibodies to mpox virus during the first month after vaccination

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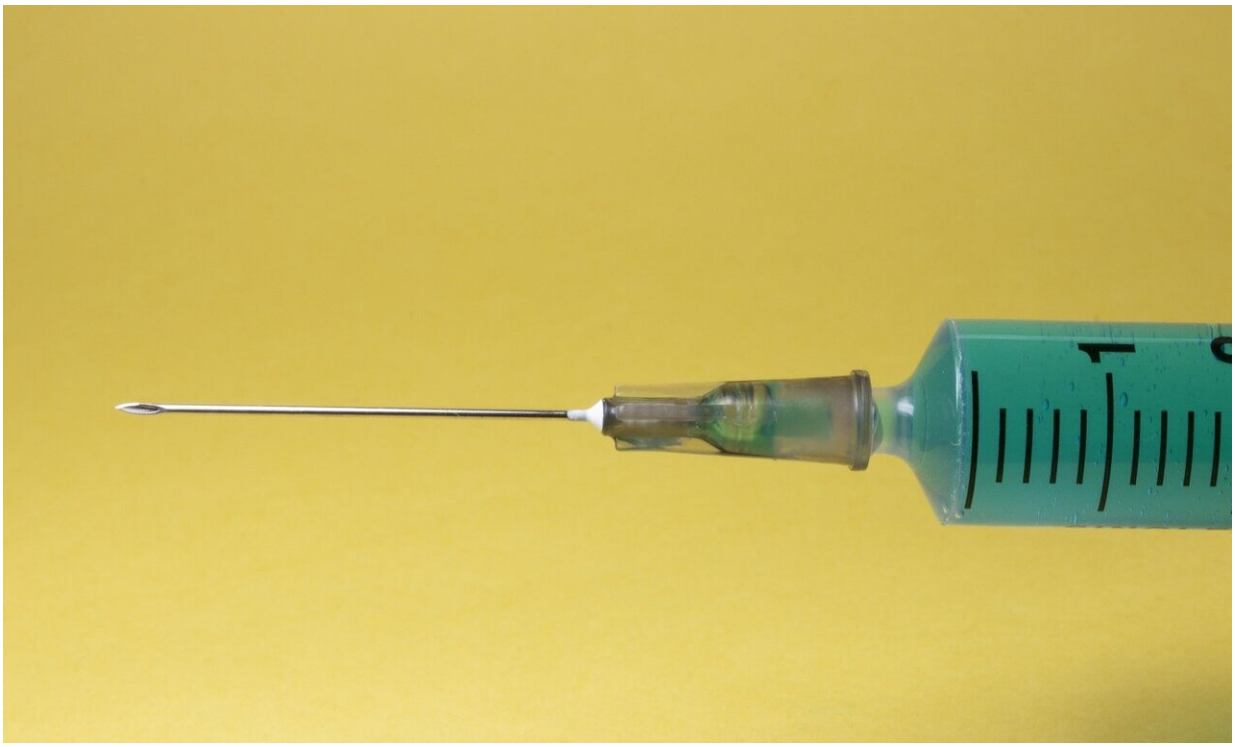

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New research to be presented at this year's European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2024) in Barcelona, Spain (27–30 April) shows that even in men who receive two doses of mpox vaccine intradermally, their level of antibodies to the virus falls to low or zero within the first few months if they have not received a previous smallpox vaccine.

Previous smallpox vaccination contributes significantly to higher neutralizing antibodies following first MVA-BN dose.

The authors, who include Dr. Klara Sonden, deputy state epidemiologist of the of Public Health Agency of Sweden and affiliated to Karolinska Institute, Stockholm, Sweden, says that their study shows that booster vaccination may be needed long-term for such individuals, and that scientific evidence is needed for the background to any decisions.

Since May 2022, an mpox outbreak has emerged globally, spreading mainly among men who have sex with men (MSM). It was classified as a Public Health Emergency of International Concern (PHEIC).

In Sweden, a vaccine against smallpox based on the live Modified Vaccinia Virus Ankara (MVA-BN), has been offered intradermally to risk groups. Intradermal administration means 0.1 ml in the skin, one-fifth of the dose needed for subcutaneous administration. This was used as a dose-saving strategy as supplies were initially limited.

The vaccine has been shown to be efficacious in studies using real-world data from the 2022 and onward outbreak among MSM, with limited number of breakthrough infections and milder disease reported when breakthrough infections occur so far. The aim of this cohort study was to assess dynamics of, and factors affecting neutralizing antibodies against

mpox virus (MPXV) following MVA-BN vaccination.

A total of 100 MSM attending the sexual health clinic "Venhälsan," Stockholm, Sweden, eligible to receive the vaccine MVA-BN were included in the study. Following the initial serum sample drawn before dose 1, serum samples were further collected before dose 2, and 28 days and three months after the second dose.

These samples were tested to establish titers (levels) of MPXV-neutralizing antibodies. Titers were compared in individuals with or without previous smallpox vaccination and patients with past natural infection were included as positive controls.

Ten individuals were of uncertain status regarding smallpox vaccination (due to being born in many different countries in the time period 1977-1980 when vaccination was de-escalated globally) and 23 individuals were previously smallpox vaccinated. The other 67 individuals had no history of smallpox vaccination.

A total of 312 samples from four time points from the 100 individuals included in the study were analyzed. In addition to the study population, anonymized age and sex matched controls from blood donors were included as negative controls (n=20) and previously MPXV-infected individuals as positive controls (n=20). The controls gave one blood sample each.

Within the study group, previous smallpox vaccination was associated with significantly higher antibody titers, and 15/23 of these individuals had pre-existing neutralizing antibodies (i.e., the B-cell memory was still present thanks to their previous smallpox vaccination).

Among those without prior smallpox vaccination, fewer than half of the group showed any detectable neutralizing antibodies at all 28 days after

the second vaccination, with those who did exhibit responses having a median titer (standard unit of measurement of antibodies) of 20. In contrast, for previously vaccinated individuals, the median titer 28 days after a single dose of the MVA-BN vaccine was 40.

The authors say, "Our findings corroborate other studies showing that mpox vaccination results in neutralizing antibodies only in a proportion of vaccinees, and that a significant decline occurs already during the first month post-vaccination Immunity after previous MPXV infection mounts a higher and more robust neutralizing response. In conclusion, the findings merits the study of booster doses."

They continue: "Our results indicate a rapid decline in neutralizing antibodies after two doses and are in line with other recent studies. These results, together with the continued spread of mpox in MSM populations in Europe has prompted the consideration of a booster dose. Such a recommendation needs to be based on scientific evidence.

"However, as far as we know, no clinical trial has studied or is studying a 3rd MVA-BN dose (from an analysis of clinicaltrials.gov March 2024), but a booster dose is common practice for inactivated vaccines. The MVA-BN is a live, non-replicating vaccine and therefore likely equivalent to an inactivated vaccine.

"Studies are essential to inform public health policy, and the largest STI clinic in Sweden is planning to perform a randomized clinical trial of a booster dose with immunological parameters as the primary outcome in the comparison with those who have had the two doses of the regular full 0.5 subcutaneous dose (sc) (0.5ml), two doses of the dose-saving intradermal dose (id) (0.1ml), or one dose sc/one dose id, and those with no booster dose."

They add that despite this, the mpox cases in Sweden have been few and

mostly imported during 2023 (12 cases) and 2024 (5 cases) and the vast majority have been among unvaccinated individuals.

Data collection is ongoing regarding the occurrence of breakthrough infections in Sweden. Breakthrough cases have been reported in the scientific literature among individuals that have received different vaccination strategies (i.e. sc/sc, id/sc, id/id).

Dr. Sonden concludes, "The results presented here indicate that long-term protective immunity might need a booster dose for its maintenance. Since the current situation regarding mpox in Sweden is stable with minimal transmission any change in policy should be backed by results from clinical trials.

"Currently we will focus on finding unvaccinated individuals who are at risk of getting mpox and offer them vaccination, and we believe that this as well as the previously administered vaccinations will contribute to lowering the risk for new outbreaks of mpox in Sweden in future."

Provided by European Society of Clinical Microbiology and Infectious Diseases

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