

Intradermal vaccination, a promising solution for Mpox immunization

Arya Mehta | Amélie Donck | Danielle Pasmans | Momen Rbeihat | Manon Randrianantoandro | Koen CL Beyers | Vanessa Vankerckhoven
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MPOX HISTORY

In the 1950s, the mpox virus was identified for the first time in lab monkeys – hence the name, yet African rodents most likely are the actual carriers of the virus and responsible for its spread [1].

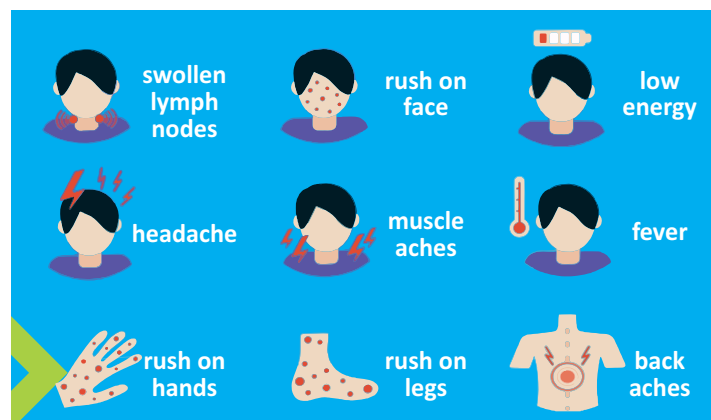
Mpox, formerly known as monkeypox, is a zoonotic viral infection meaning it can spread from animals to humans. The virus is a double stranded DNA virus, part of Poxviridae family, Chordopoxvirinae subfamily, and Orthopoxvirus genus [2]. It wasn't until the early 1970s that the first confirmed case of the mpox virus in humans was seen. It was initially suspected to be Smallpox, but was later confirmed to be mpox [3].

There was no foremost consideration of the potential risks that the virus could have, potentially due to the confirmed infections being underreported as most cases were in rural African contexts with limited healthcare access [3].

SYMPTOMS & DETECTION

The manifestations of mpox in humans are similar to those of smallpox disease. Presence of the virus can be suspected with the sudden onset of fever, followed by an eruption of vesiculopustular rash that predominates the face, palms, and soles of the feet.

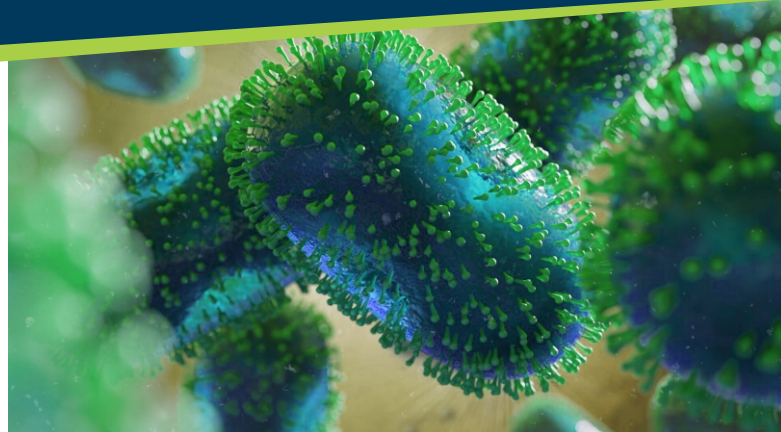
The presence of a minimum of 5 smallpox-type scabs may raise the suspicion of mpox virus; however, the virus can manifest with various dermatological findings and clinical presentations [2]. To confirm this suspicion, laboratory confirmation from skin lesion samples through positive IgM antibody, PCR, or virus isolation is needed [2,4].



EPIDEMIOLOGY & TRANSMISSION

Transmission of the virus to humans can occur through an infected animal, and this can be through direct or indirect contact with the animal's bodily fluids, skin lesions, or respiratory droplets.

Due to a lack of herd immunity to Orthopoxvirus, the threat of mpox spread among humans is now considered very high [5].



The infected individual may have a mpox rash, fever, body ache. Contact transmission includes and is not limited to face-to-face, skin-to-skin, mouth-to-mouth, or mouth-to-skin contact, with sexual contact being the main form of transmission [6].

Although mpox is not considered to be a sexually transmitted infection (STI), mostly men having sex with men (MSM) have been affected in Europe and US in 2022, but cases now start to surge among pediatric and other populations as well. Importantly, recent findings by the Institute for Tropical Medicine in Belgium, indicates that the virus might be transmitted to close contacts in the absence of symptoms and identification and isolation of symptomatic individuals may not suffice to contain the outbreak [7].

Mpox primarily occurs in tropical rainforest areas of Central and West Africa, with the Democratic Republic of Congo (DRC) being an important epicenter. The virus is endemic in the DRC, largely due to the dense tropical rainforests that facilitate the transmission of the virus from wildlife to humans. People living in remote areas, where healthcare access is limited, are particularly vulnerable. Two clades have been identified: Clade I, the Congo Basin Clade and Clade II, the West Africa clade [8].

Mpox in Democratic Republic of Congo (DRC)

Mpox has been a persistent public health issue, particularly in the Democratic Republic of the Congo (DRC) and neighbouring countries such as Burundi, Kenya, Rwanda and Uganda. Reasons for ongoing challenges with Mpox in the region include poor healthcare infrastructure, lack of public health knowledge on prevention methods, and conflict and political instability in the area.



From the beginning of 2022 to the end of January 2025, the global mpox outbreak has resulted in almost 130 000 confirmed cases and more than 283 deaths across 130 countries [8], [9].

The DRC's ongoing challenges with mpox are exacerbated by several factors. The healthcare infrastructure is weak, making it difficult to diagnose and manage cases effectively. There is also a lack of widespread public health education, which means many people are unaware of the ways to prevent infection. Additionally, ongoing conflict and political instability in various regions hinder public health efforts and exacerbate the spread of the disease.

To address these challenges, the World Health Organization (WHO) has developed a strategic preparedness, readiness, and response plan for mpox.

This plan includes enhancing surveillance, improving diagnostic capabilities, and conducting vaccination campaigns in affected areas. The aim is to detect and respond to mpox outbreaks quickly and effectively to prevent further spread and mitigate the impact on affected communities.

VACCINATION

Vaccination is considered a key strategy to prevent mpox outbreaks. Imvanex (Bavarian Nordic A/S), branded as Jynneos in the US and Imvamune in Canada, is the only vaccine authorized in the EU for the prevention of smallpox, mpox and disease caused by vaccinia virus in adults. Imvanex is a non-replicating live attenuated third generation vaccine based on the Modified Vaccinia Ankara – Bavarian Nordic vector (MVA-BN) containing no less than 5×10^7 infectious units per 0.5 mL dose presented in a single-dose type I glass vial for subcutaneous (SC) administration. It is given as two doses at least 28 days apart [10].

Today several types of vaccine candidates with different strategies for mpox, including inactivated, live-attenuated, virus-like particles (VLPs), recombinant protein, nucleic acid, and nanoparticle-based vaccines are being developed and investigated [11]. Given the worrying trends in the disease's spread, WHO invites mpox vaccine manufacturers for emergency evaluation.

INTRADERMAL VACCINATION

Vaccines delivered through the intradermal (ID) route have been proven to be non-inferior or even superior when compared to the intramuscular (IM) or SC routes [9]. This is due to the skin offering a rich immunological environment for the administration of the vaccine's antigen. The richness of skin with antigen-presenting cells compared to levels in the muscle and subcutaneous tissue highlights the dose-sparing properties of an ID administered vaccine as less of the dose is needed (1/3 to 1/10th).

This consequently leads to lower cost, higher availability of doses and easier storage and distribution of vaccines. Together, ID can improve the availability of vaccines, particularly when fighting a growing outbreak like mpox [12].

Intradermal vaccinations are often performed using the Mantoux technique Figure 1. This technique encompasses a usability rattle; it is a challenging technique which depends on specialized medical personnel to administer the vaccine correctly to the dermal layer of the skin.

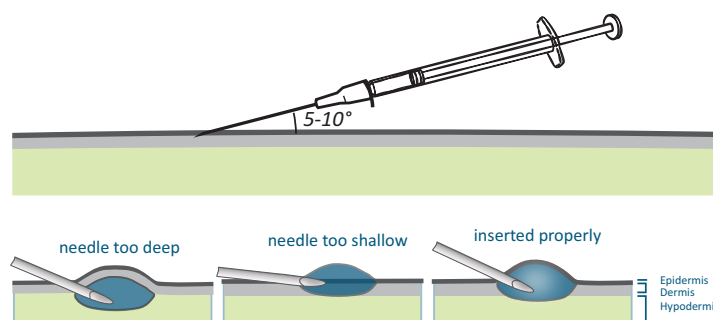


Figure 1: Mantoux technique with possible incorrect administrations of the injection.

This traditional technique of administering intradermal injections is performed with a syringe and needle parallel to the skin, with an angle of 10 to 15 degrees. It's perceived as painful by the vaccinee, and it has been shown that over 70% over the injections were incorrectly performed [13].

Intradermal delivery of vaccines, allowing antigen sparing, is approved for several vaccines, notably BCG (tuberculosis vaccine), influenza and rabies vaccines. In 2022, both the U.S. Food and Drug Administration (FDA) as well as the European Medicines Agency (EMA) declared an Emergency Use Authorization (EUA) for ID injection of the MVA-BN vaccine using 1/5th of the dose (0.1 mL) of the standard SC dose [14, 15]. The 2-dose regimen remains [10].

The study by Frey et al. (2023) confirmed that ID injection is safe according to the FDA's toxicity grading scale and did not lead to unacceptable local reactions. The median duration of erythema was shorter by 1 day in the ID group compared to the SC group. Furthermore, the ID route allows for dose sparing of the prophylactic MVA-BN vaccine against mpox; 80% of the vaccine dose was spared, as compared with the SC route [16]. The results also confirm those of 2015, whereby a comparable humoral immunogenicity was demonstrated in healthy adults when MVA-BN was given as a standard SC dose or as 1/5th of a dose administered ID [17]. Additionally, a 2024 Australian study involving nearly 10,000 doses found no significant difference in adverse events between ID and SC administration, though age-related variations in reactions were observed [18].

During the 2022 vaccination campaign, the MPOX Vaccine Lazio Study Group compared the immunogenicity and reactogenicity of the ID and SC route of administration and found that the ID route elicited higher titers of MPXV-specific IgG and nAbs than the subcutaneous (SC) route without evidence for a difference in cellular response one month after the complete vaccination cycle. Additionally the ID dose-sparing strategy was proven to be safe.

Real world safety data collected by the manufacturer until the end of 2023 revealed that the percentage of reported syncope adverse events following ID administration was increased compared to other routes of administration. The cause for a potential difference in syncope between routes of may be a response to greater pain or longer duration of the application experienced with the traditional ID route. Noteworthy, Mazzotta et al did not observe these events during the mpox vaccination campaign in Italy over 2022-2023. [19].

VAX-ID® FOR INTRADERMAL DELIVERY OF MPOX VACCINE

VAX-ID® is an award-winning patented medical device for intradermal injection Figure 2. VAX-ID® offers a promising solution for standardized, reliable, and user-independent injection.



Figure 2: The VAX-ID® device

The device elicits less pain during injection (and can be completely painless, depending on the viscosity of the vaccine being administered) due to its thin and short needle and smooth application technique Figure 3 [20]. During an investigational study, conducted in healthy subjects, nearly no pain was reported using VAX-ID. Additionally, the duration of the injection time with VAX-ID was perceived as being shorter compared to intramuscular injection with needle and syringe. The lack of pain and shorter duration may eliminate the risk for fainting [20].

Additionally, Van Mulder et al., demonstrated that ID injection with 1/4th of the IM dose using VAX-ID® had a non-inferior immunogenicity and safety when compared to IM using a Hepatitis B vaccine in healthy volunteers, and its design features were seen as an encouraging alternative for providing ID vaccination [21].

CONCLUSION

Intradermal vaccination offers a solution to limit the amount of vaccine dose (up to 1/5th) needed to elicit non-inferior immunogenicity to the full dose, thereby decreasing dosage volumes kept in the cold chain, and increasing vaccine availability. Intradermal vaccination is thus particularly attractive for use in mass vaccination campaigns or outbreaks like now seen with mpox, or for vaccines that are expensive or in short supply thereby aiding in the rising demand for faster access to vaccination. VAX-ID® can offer a solution in ease of use and standardization of the ID injection aiding in reliable ID administration by health care professionals.

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Figure 3: VAX-ID Instruction for Use

