Intradermal Vaccination, a Promising Solution in the Mpox Outbreak

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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 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].
Recently, the WHO announced their use of the substitutive "mpox" for the current outbreak of monkeypox virus. The recommendation to use this synonym took place to counteract the stigmatizing and racist online language, which have been reported frequently to the WHO. A transition period of one year will allow for using both synonyms interchangeably; however, following the transition period the "mpox" term will be replacing the monkeypox. The transition period is adopted to alleviate turbulence that might be caused from the disease name change while in the middle of a worldwide outbreak, as proposed by experts [16].

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 vesicular-pustular 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 is possible through an infected animal, and this can be through direct or indirect contact with the animal's bodily fluids, skin lesions, or respiratory droplets. Previously, it was suspected that transmission from human-to-human was very limited. Nevertheless, due to a lack of herd immunity to Orthopoxvirus, the threat of mpox spread among humans is now considered very high [5]. This helps explain the current emerging mpox outbreak that is spreading worldwide, with transmission happening as a result of close contact with an infected individual. The infected individual may have a mpox rash, contact 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 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].

VACCINATION

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 x 107 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 [8].

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 intradermally-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 [9].
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.

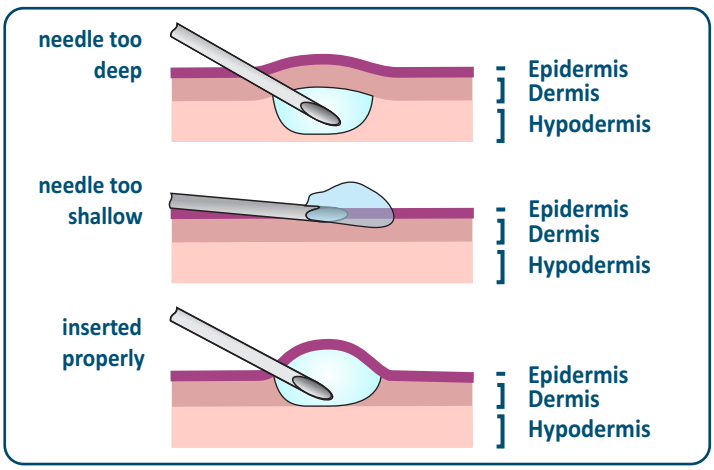

Figure 1: Mantoux technique with possible incorrect administrations of the injection.

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 [10].

Intradermal delivery of vaccines, allowing antigen sparing, is approved for several vaccines, notably BCG (tuberculosis vaccine), influenza and rabies vaccines. Recently, the 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 [8, 11]. The 2-dose regimen remains [12]. A study in healthy adults demonstrated comparable humoral immunogenicity when MVA-BN was given as a standard SC dose or as 1/5th of a dose administered ID. The exact level of protection and duration of protection afforded by the vaccine regimens are unknown [13].

EMA notes that it is essential to recognize the importance of correct ID administration to ensure that immune responses will be comparable to those achieved with a standard SC dose. Therefore, it is recommended that ID delivery of reduced dose of Imvanex is performed by professionals with ID vaccine administration experience.

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. 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 [14]. 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 [15].

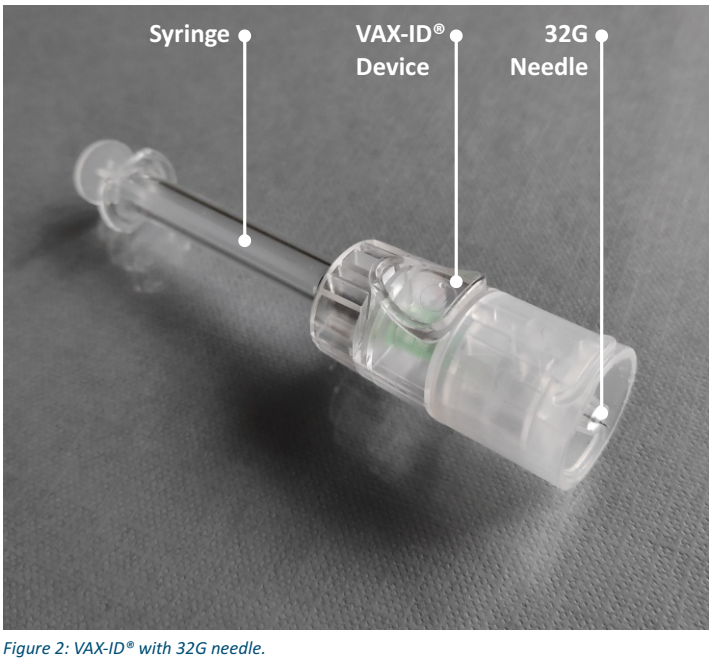

Figure 2: VAX-ID® with 32G needle.

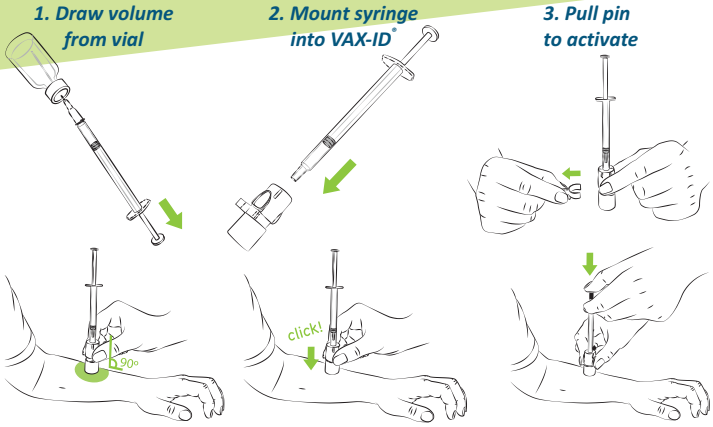

Figure 3: Instruction on the use of VAX-ID® for intradermal drug/vaccine delivery.

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.

REFERENCES

1. Monkeypox. Institute of Tropical Medicine Antwerp. (n.d.). Retrieved August 22, 2022, from https://www.itg.be/E/monkeypox

2. Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis. 2022;16(2):e0010141. Published 2022 Feb 11. doi:10.1371/journal.pntd.0010141

3. Moore MJ, Rathish B, Zahra F. Monkeypox. In: StatPearls. Treasure Island (FL): StatPearls Publishing; July 16, 2022

4. Laboratory testing for the Monkeypox virus - world health organization. (n.d.). Retrieved August 22, 2022, from https://apps.who.int/iris/bitstream/handle/10665/354488/WHO-MPX-Laboratory-2022.1-eng.pdf

5. Grant R, Nguyen LL, Breban R. Modelling human-to-human transmission of monkeypox. Bull World Health Organ. 2020;98(9):638-640. doi:10.2471/BLT.19.242347

6. World Health Organization. (n.d.). Monkeypox. World Health Organization. Retrieved August 19, 2022, from https://www.who.int/news-room/questions-and-answers/item/monkeypox?gclid=EAIaIQobChMI5aC45OvS-QIVweh3Ch0vAJHEAAYASACEgLnS_D_BwE

7. De Baetselier, I., Van Dijck, C., Kenyon, C., Coppens, J., Van den Bossche, D., Smet, H., Vanroye, F., Liesenborghs, L., Ramadan, K., Platteau, T., Van Looveren, K., Baeyens, J., Van Hoyweghen, C., Mangelschots, M., Coppens, S., Heyndrickx, L., Michiels, J., De Block, T., Manoharan-Basil, S., … Van Esbroeck, M. (2022, June 21). Asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium. SSRN. Retrieved August 22, 2022, from https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4142074

8. Ema. (2022, July 29). EMA recommends approval of IMVANEX for the Prevention Monkeypox Disease. European Medicines Agency. Retrieved August 22, 2022, from https://www.ema.europa.eu/en/news/ema-recommends-approval-imvanex-prevention-monkeypox-disease

9. Hickling JK, Jones KR, Friede M, Zehrung D, Chen D, Kristensen D. Intradermal delivery of vaccines: potential benefits and current challenges. Bull World Health Organ. 2011;89(3):221-226. doi:10.2471/BLT.10.079426

10. Micheels P, Goodman L. Injection Depth in Intradermal Therapy: Update and Correction of Published Data. J Drugs Dermatol. 2018;17(1):88-96.

11. Commissioner, O. of the. (n.d.). Monkeypox update: FDA authorizes emergency use of JYNNEOS vaccine to increase vaccine supply. U.S. Food and Drug Administration. Retrieved August 19, 2022, from https://www.fda.gov/news-events/press-announcements/monkeypox-update-fda-authorizes-emergency-use-jynneos-vaccine-increase-vaccine-supply

12. Ema. (2022, August 19). Ema's emergency task force advises on intradermal use of Imvanex / Jynneos against Monkeypox . European Medicines Agency. Retrieved August 22, 2022, from https://www.ema.europa.eu/en/news/emas-emergency-task-force-advises-intradermal-use-imvanex-jynneos-against-monkeypox

13. Frey SE, Wald A, Edupuganti S, et al. Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects. Vaccine. 2015;33(39):5225-5234. doi:10.1016/j.vaccine.2015.06.075

14. Van Mulder TJ, Verwulgen S, Beyers KC, et al. Assessment of acceptability and usability of new delivery prototype device for intradermal vaccination in healthy subjects. Hum Vaccin Immunother. 2014;10(12):3746-3753. doi:10.4161/21645515.2014.979655

15. Van Mulder TJS, Withanage K, Beyers KCL, Vankerckhoven VVJ, Theeten H, Van Damme P. Immunogenicity and safety of intradermal delivery of hepatitis B booster vaccine using the novel drug delivery device VAX-ID™. Vaccine. 2019;37(4):581-586. doi:10.1016/j.vaccine.2018.12.016

16. World Health Organization. (n.d.). WHO recommends new name for Monkeypox disease. World Health Organization. Retrieved December 9, 2022, from https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease