

Intradermal vaccination: a key strategy for a OneHealth Rabies eradication approach to reach zero by 30 goal

Arya Mehta | Danielle Pasmans | Amélie Donck | Koen Beyers | Vanessa Vankerckhoven

Idevax BV, Belgium September 28, 2024

INTRODUCTION

Rabies is a zoonotic viral disease that can be transmitted between animals and humans. This disease causes approximately 59,000 deaths each year and is found in over 150 countries. Most cases are transmitted by dogs and occur in Africa and Asia. Around 40% of the affected individuals are children under the age of 15 (1).

Once clinical symptoms of rabies appear in a person, the disease becomes almost invariably fatal, with an extremely high fatality rate of virtually 100%. In many instances, up to 99% of cases, dogs are identified as the primary cause responsible for transmitting the rabies virus to humans (1).

Fortunately, human rabies can be prevented by vaccines. Since the pioneering work of Pasteur and Roux in 1885, safe and efficacious Rabies vaccines have been developed (2).

Today, 27 vaccines are currently available on the global market. Only 4 of the 27 vaccines are prequalified, representing 14% of the total supply and allowing for limited flexibility in procurement.

“ONE HEALTH APPROACH” TO REACH “ZERO BY 30 GOAL”

Unlike numerous other diseases, the tools needed to eliminate dog-mediated rabies (in animals and humans) already exist (1). In 2018, the World Organization for Animal Health (WOAH), the Food and Agriculture Organization of the United Nations (FAO), and the Global Alliance for Rabies Control (GARC), jointly launched a Global Strategic Plan for the eradication of human rabies deaths caused by dogs worldwide by 2030, and it is guided by a “One Health Approach” (3).

Wide-spread dog vaccination initiatives, which address the disease at its source in animals, have shown success in many regions across Africa, Asia, Europe, and America (1).

“HUMAN RABIES is 100% VACCINE PREVENTABLE”

Protection against rabies is very efficient and can be achieved by either of two ways: pre-exposure vaccination (PrEP) for populations at high risk of exposure or post-exposure prophylaxis (PEP) following a transdermal animal bite. (4)

Pre-exposure vaccination (PrEP)

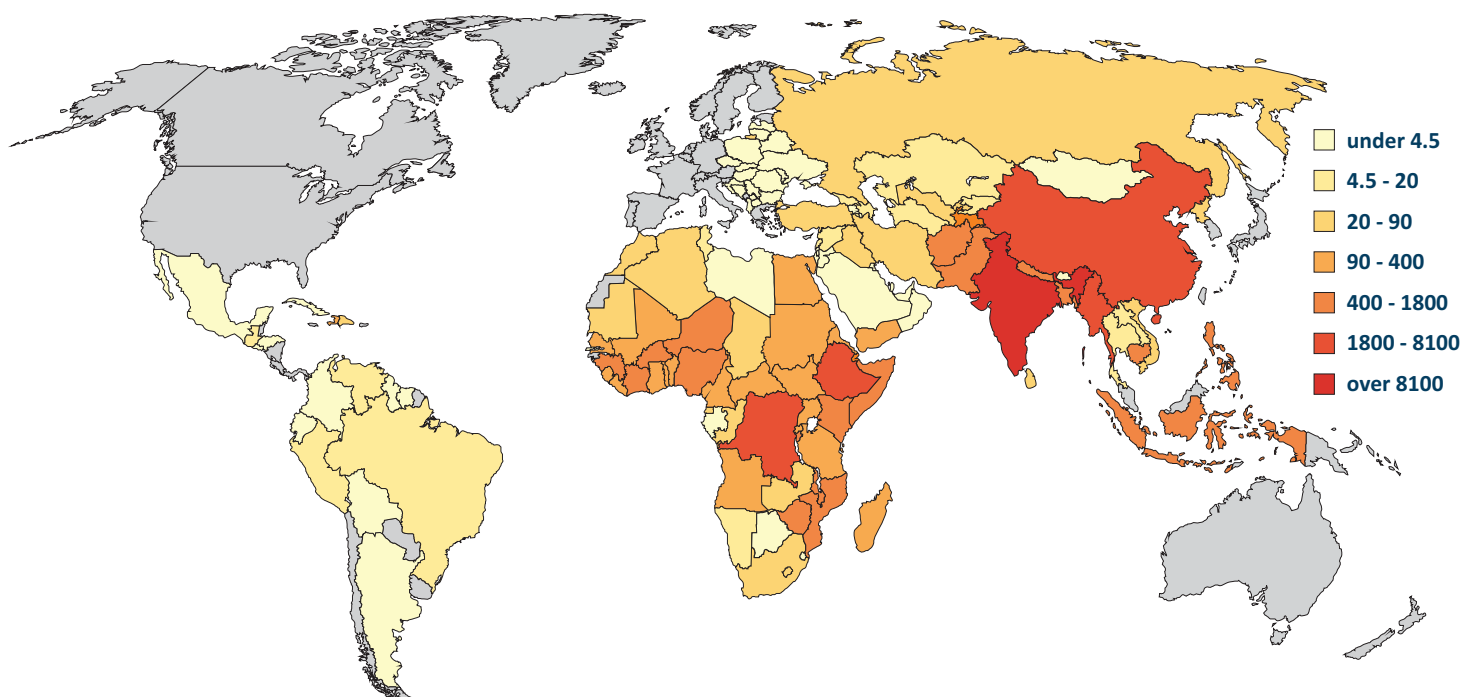
High-risk groups for rabies exposure include animal healthcare personnel, wildlife officers, veterinarians, veterinary students, hospital healthcare workers, certain laboratory workers, and military personnel particularly in rabies endemic areas. (4,5)

Pre-exposure prophylaxis, consists of administering a series of intramuscular or intradermal injections of rabies vaccine to prime the immune system. This enables a fast recall of memory immune responses once a person is re-exposed to the virus. (6)

Post-exposure prophylaxis (PEP)

The relatively extended incubation period, spanning 1–3 months for most cases, allows for the timely implementation of highly effective PEP promptly after exposure, including: (1)

- Washing and cleaning of the wound.
- A series of intradermal or intramuscular rabies vaccine administrations promptly after an exposure.
- If deemed necessary, administering Rabies Immunoglobulin (RIG) into and around the wound.



PMID: 30150166

As prompt PEP following severe exposures is 100% effective in preventing rabies, deaths occur mainly in those who cannot access timely and effective PEP (1).

PEP, however, requires several vaccination sessions and, in certain cases, the availability of immediately acting immunoglobulins (RIG). These immunoglobulins are costly and not always available in LMICs. This procedure is simplified if the patient got PREP before the incident.

Rabies pre-exposure prophylaxis (PrEP) greatly simplifies PEP: RIG is no longer needed, and the number of rabies PEP vaccine doses required is reduced (4).

INTRADERMAL VACCINATION AS COST-SAVING AND DOSE-SPARING ALTERNATIVE

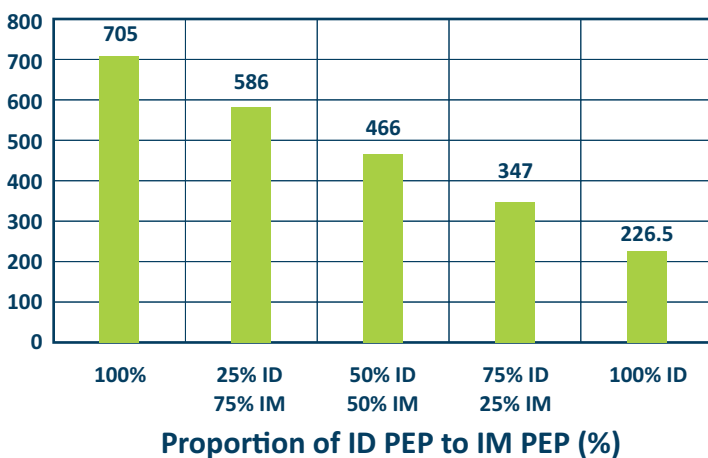
To address the issue of frequent vaccine shortages and cost, intradermal administration of rabies vaccines provides a **cost-saving** and **dose-sparing** alternative to intramuscular vaccination.

Compared to standard intramuscular vaccination, intradermal vaccination offers an equally safe and immunogenic alternative, reducing the vaccine volume required and consequently lowering the direct vaccine cost by 60–80%. (6)

As the cost of vaccines for intramuscular administration limits their widespread use in many areas where rabies is present, the WHO also promotes the use of intradermal administration of these vaccines as a safe, immunogenic and cost- and dose-sparing alternative to intramuscular administration. Intradermal administration is cost-effective for both PrEP and PEP. (7)

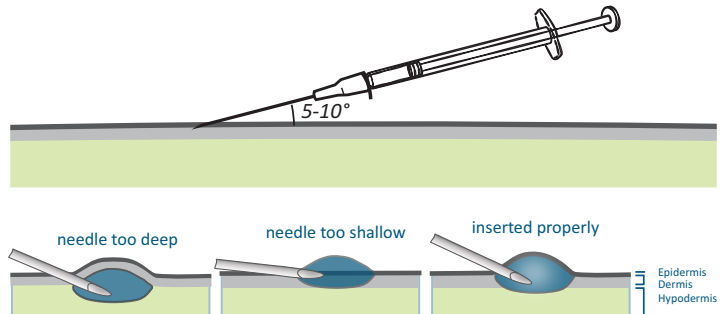
The table below illustrates the estimated cost when using varying proportions of intradermal and IM rabies PEP for 4 million dog bite patients. (2)

Estimated cost of PEP provision in millions US\$



Of the 27 vaccines currently available on the global market, 16 are labelled for intradermal administration in addition to intramuscular. Three of the four prequalified vaccines are indicated for intradermal administration.

The current standard of care in intradermal administrations is the so-called Mantoux technique which requires a substantial level of training, as incorrect injection can lead to a lack of efficacy and vaccination failures. (8) Additionally, it poses a standardization challenge as it has been shown that over 70% of the injections were incorrectly performed and the injection is perceived painful for the patients. (9)



Several recent publications showed that VAX-ID®, a novel intradermal drug delivery device offers a promising solution for standardized, reliable, user-independent injection (10).



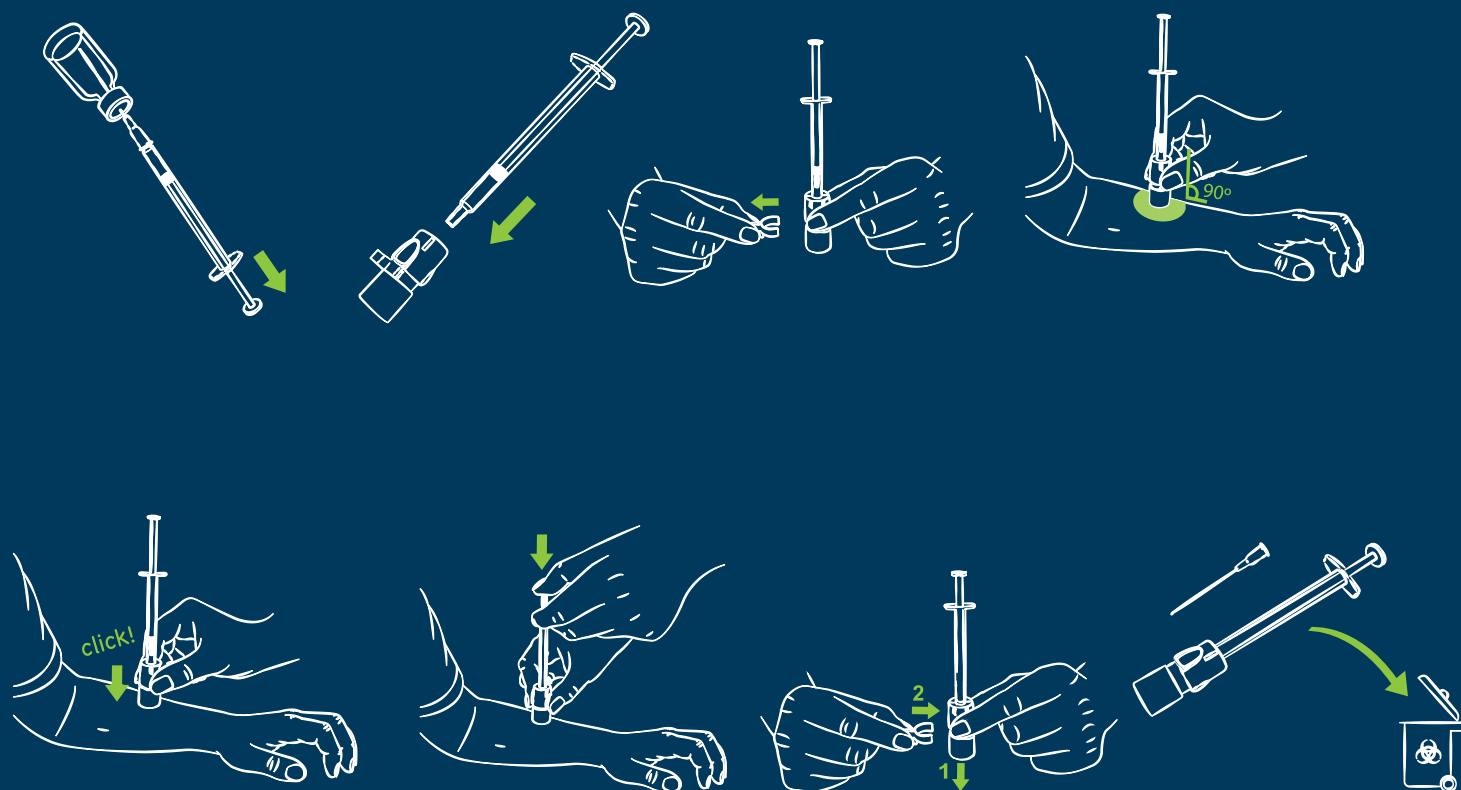
VAX-ID® device

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 (10).

CONCLUSION

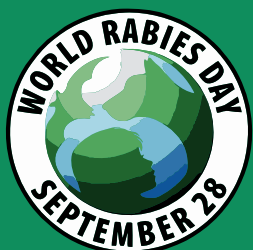
Intradermal vaccination offers a solution to limit the amount of vaccine dose (up to 1/5th) needed to elicit non-inferior immunogenicity to the full dose, thereby decreasing dosage volumes kept in the cold chain, and increasing vaccine availability. Intradermal vaccination is thus particularly attractive for vaccines such as the rabies vaccination where multiple doses may be required or where supply may be limited. This vaccination method could be a key tool to help achieve the 'OneHealth Rabies eradication approach to reach zero by 30' goal.

VAX-ID® can offer a solution in ease of use and standardization of the intradermal injection aiding in reliable intradermal administration by health care professionals.



REFERENCES

1. Zero by 30: the global strategic plan to end human deaths from dog-mediated rabies by 2030. June 2018. [Zero by 30: the global strategic plan to end human deaths from dog-mediated rabies by 2030 \(who.int\)](https://www.who.int/publications/i/item/zero-by-30-the-global-strategic-plan-to-end-human-deaths-from-dog-mediated-rabies-by-2030), last accessed September 2024
2. Gongal G et al. Introduction of intradermal rabies vaccination - A paradigm shift in improving post-exposure prophylaxis in Asia. *Vaccine*. 2019. PMID: 30150166.
3. United Against Rabies (UAR) - <https://www.who.int/initiatives/united-against-rabies>; last accessed September 2024
4. Van Nieuwenhove MDM et al. Timing of Intradermal Rabies Pre-exposure Prophylaxis Injections: Immunological Effect on Vaccination Response. *Mil Med*. 2019. PMID: 31004174.
5. Kewcharoenwong C et al. One-dose intradermal rabies booster enhances rabies antibody production and avidity maturation. *Med Microbiol Immunol*. 2024. PMID: 38761268
6. Kessels JA et al. Pre-exposure rabies prophylaxis: a systematic review. *Bull World Health Organ*. 2017 Mar. PMID: 28250534.
7. WHO expert consultation on rabies: third report: WHO Technical Report Series N°1012. 2018. <https://www.who.int/publications/i/item/WHO-TRS-1012>, last accessed September 2024
8. Guide to introducing human rabies vaccine into national immunization programmes. July 2022. <https://www.who.int/publications/i/item/9789240052499> last accessed September 2024.
9. Micheels P & Goodman L. *J Drugs Dermatol*. 2018. PMID: 29320593
10. <https://idevax.com/dataroom/>



BREAKING RABIES BOUNDARIES

