Unlocking Mucosal Immunity: The Untapped Potential of Intradermal Vaccination

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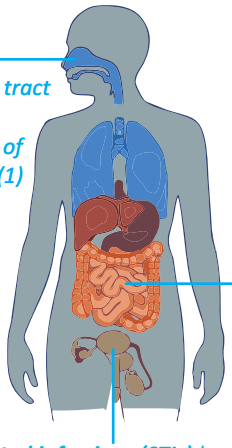
The burden of infectious diseases caused by mucosal pathogens

Mucosal tissues in the gastrointestinal, respiratory, and urogenital tracts are prominent sites of pathogen entry and often associated with tumor development (1).

Since more than 90% of human pathogens exploit these surfaces, inducing mucosal immunity is critical for preventing transmission (2). Reflecting this vulnerability, respiratory, enteric and sexually transmitted infections rank among the leading causes of death worldwide.



Respiratory *Lower respiratory tract infections are the 4th leading cause of death worldwide (1)*

Enteric *pathogens causing diarrheal disease are the eighth leading causes of death worldwide, with mostly children at risk (1)*

Sexually transmitted infections (STIs) *have a profound impact on sexual and reproductive health worldwide and can have serious consequences beyond the immediate impact of the infection itself. (WHO)*

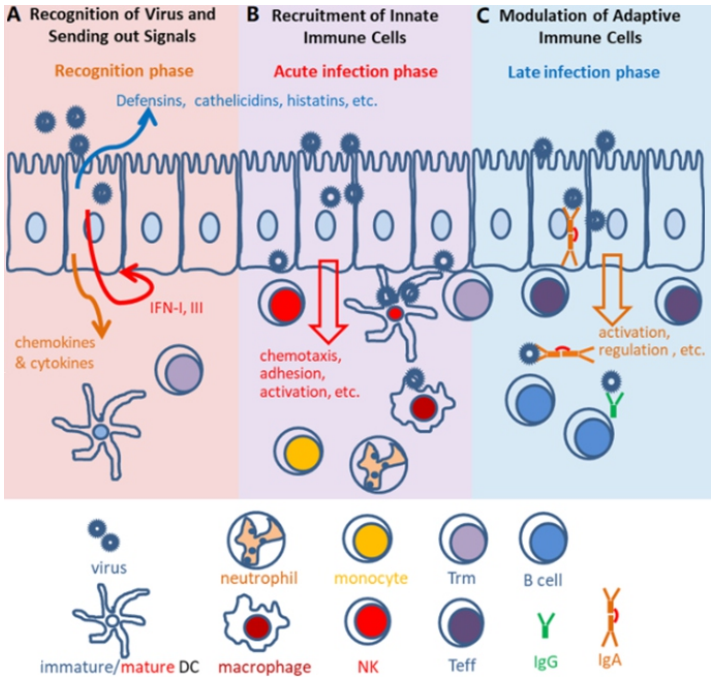
Adapted from Lavelle EC, et al. Nat Rev Immunol. 2022. PMID: 34312520.

Despite the effectiveness of vaccines in controlling infectious diseases, the global burden of mortality and morbidity caused by mucosal pathogens remains unacceptably high (1).

This is largely related to most vaccines are administered through the parenteral route, which elicits robust systemic humoral response but induces only weak T-cell-mediated immunity and poor mucosal protection (3).
Consequently, there is an urgent need for new and improved vaccines to combat various respiratory and enteric pathogens, as well as sexually transmitted infections and oncogenic viruses that exploit access through the mucosal surfaces (1).

The mucosal immune system: a complex immune network

The physical, chemical, biological, and immunological barriers of the mucosa plays a key role as a first line host defense against pathogens (4). The mucosal immune system consists of a complex network of innate and adaptive immune components working together to maintain the integrity of the mucosal barrier and mediate immune responses to invading pathogens. A strong mucosal immunity can prevent infections across these surfaces and reduce secondary transmission of pathogens shed from mucosal sites. (2)



Yang et al, Cell & Mol Immunol 2021 PMID: 33927362
https://pubmed.ncbi.nlm.nih.gov/33927362/

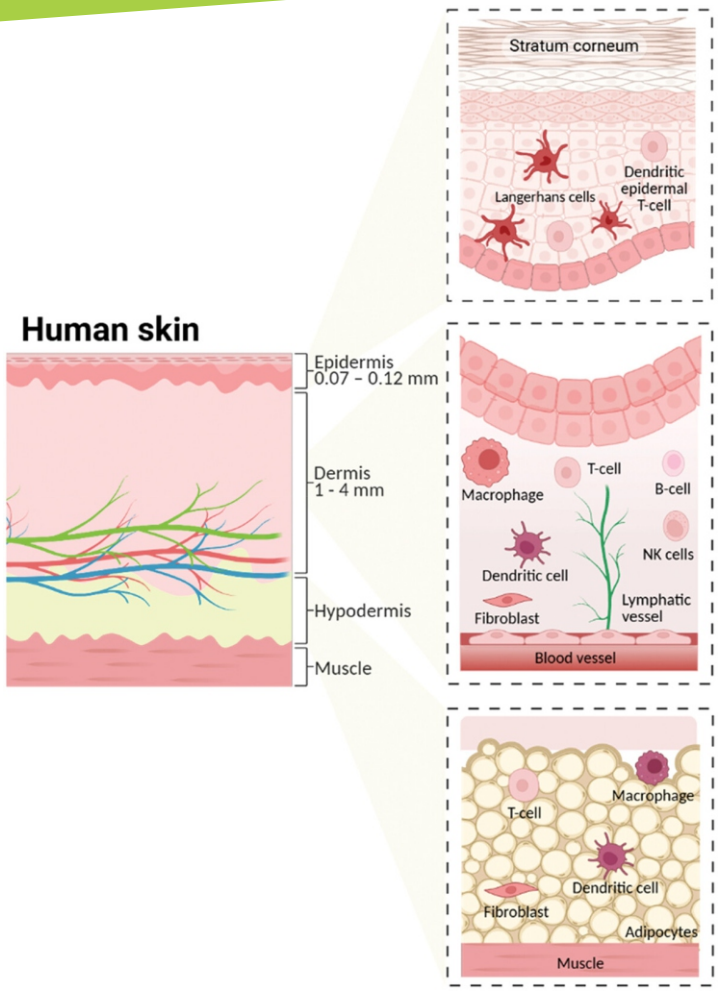
Unfortunately, the development of mucosa-targeting vaccines is challenging because the same barriers that protect against pathogens also impede traditional vaccine delivery (4).

This highlights the need for novel vaccines and vaccine strategies capable of inducing mucosal immunity through non-mucosal immunization routes (5). A recent study from the Tulane University School of Medicine has demonstrated that this non-mucosal to mucosal immunity link can be established predominantly via intradermal immunization (5).

Intradermal vaccination: an alternative vaccine delivery method

The skin consists of 3 layers: stratum corneum (SC), epidermis, and dermis of which the epidermis and dermis contain major innate immune cells: Langerhans cells (LCs), dendritic cells (DCs), macrophages, mast cells, eosinophils and a good number of T lymphocytes.

Especially the large presence of antigen-presenting cells, such as epidermal LCs and dermal DCs, in the skin explains the more potent immune response of intradermal (ID) vaccination compared to intramuscular vaccination (6).
Additionally, intradermal vaccines may also activate local innate immune cells to secret cytokines and chemokines and recruit circulating innate immune cells (6).



Verbist et al. Human Vaccines & Immunotherapeutics 2026 PMID: 41614604
https://doi.org/10.1080/21645515.2026.2619235

Several studies have shown that only a fractional vaccine dosage is required when using ID as compared to intramuscular (IM) or subcutaneous (SC) for similar immunization against Hepatitis B, Influenza, Rabies, Polio, Yellow Fever and SARS-CoV-2 (7). Moreover, the skin is easily accessible and contains components that can induce both humoral and cellular immunity (8).

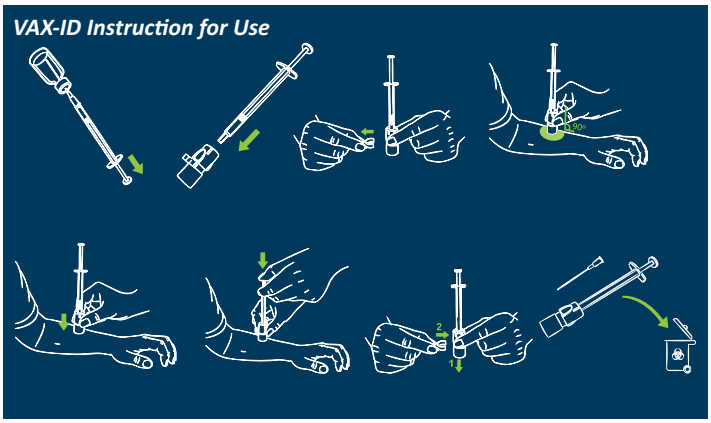
Mantoux, the traditional technique of administering ID injections is performed with a syringe and needle parallel to the skin, with an angle of 10 to 15 degrees.
Unfortunately, it's perceived as painful by the vaccinee, and it has been shown that over 70% over the injections were incorrectly performed (9)

VAX-ID®: offering reliable skin delivery of medical products

IDEVAX created VAX-ID® to overcome the challenges of the traditional Mantoux technique. Designed for simplicity and built for accuracy, VAX-ID® ensures standardized, reliable, and user-independent delivery into the dermal layer of the skin.

As an award-winning, CE-marked Class IIa medical device, VAX-ID® meets the highest European standards for quality, safety, and performance.

By combining high ease of use, a predefined penetration depth, and optimized safety features, VAX-ID® empowers clinicians to administer intradermal injections with confidence, consistency, and minimal discomfort for patients.



Conclusion

As evidence grows that intradermal vaccination can effectively activate mucosal immunity, interest in skin-based immunization continues to accelerate. VAX-ID® enables this shift by providing a consistent and accurate intradermal delivery method, solving the long-standing challenges of the Mantoux technique.

References

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