

pertinent, instigating IT surveillance systems to track antibiotics through the supply chain, monitoring pharmacy activities using mobile technologies, and educating patients on the dangers of self-medication with antibiotics. Multifaceted programmes are typically needed to change behaviour. Notwithstanding that community health campaigns are more challenging in LMICs,¹⁵ by championing pharmacists as antibiotic guardians, they can take the lead to improving antibiotic use in the community and reduce antimicrobial resistance.

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Improving human rabies post-exposure prophylaxis

In *The Lancet Infectious Diseases*, Tineke Cantaert and colleagues¹ illustrate a strong commitment in Cambodia to preventing human rabies by rapid intradermal delivery of post-exposure prophylaxis. The investigators included 116 people bitten by rabies virus-positive dogs and 20 people bitten by rabies virus-negative dogs who attended Institut Pasteur du Cambodge, Phnom Penh, Cambodia, between April 20, 2016, and Feb 9, 2018. Patients received intradermal vaccination on days 0, 3, 7, and 28, and serum samples were obtained for detection of rabies virus neutralising antibodies on days 0, 7, 28, and 42. This well designed cohort study showed that exposed people had rabies virus neutralising antibody titres after three rabies vaccine sessions (of two intradermal doses each) that

were similar to titres observed immediately before a fourth vaccine session on day 28. The authors concluded that rabies post-exposure prophylaxis could be abridged to a 1-week (three sessions of two doses on days 0, 3, and 7) intradermal regimen. Recognising the possibility of long incubation periods, the investigators contacted all patients after 1 year and found that all were still alive. These compelling data help identify the best use of human rabies post-exposure prophylaxis in developing countries, which should be used in combination with mass vaccination of dogs.

Historically, the intradermal route has been considered a favourable alternative to the subcutaneous or intramuscular delivery of immunogens during vaccination against several infectious diseases, including



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smallpox, tuberculosis, influenza, polio, and rabies.² The skin is a highly effective anatomical barrier to the surrounding environment and a functionally responsive tissue under immunological surveillance, with production of diverse antigen-presenting cells to respond to invasive pathogens.³ During the second half of the 20th century, as rabies vaccines improved gradually in potency and safety, intradermal administration became an increasingly attractive strategy to investigate heightened immunogenicity, dose sparing, and health economic benefits for both pre-exposure prophylaxis and post-exposure prophylaxis in human populations at risk, especially in low and middle-income countries.⁴⁻⁶

However, intradermal vaccination is not widely used for human rabies pre-exposure and post-exposure prophylaxis, with most regimens given intramuscularly over 2–4 weeks. Expressed limitations of intradermal vaccination include a need for a sizeable patient pool, decentralised clinics, and clinical skills for intradermal delivery; a disinclination to accept off-label use of licensed products; a need for improved devices for vaccine administration to infants and children; and potential for increased local reactogenicity compared with other parenteral routes.^{2,3,7,8} Overcoming these perceptions is crucial for widespread use of intradermal vaccination.

One reason for the lack of intradermal regimens for rabies prevention might be that human exposure to rabies virus is lower in Europe and North America owing to elimination of canine rabies in those settings. However, this is not the case in Africa and Asia, where canine rabies is enzootic and shortage of biologics is common. Training of staff in these settings by workers who are adept at BCG vaccine administration and tuberculin skin-testing could broaden the use of intradermal vaccination.

Approval of intradermal regimens by regulatory bodies should follow the traditional pathways for intramuscular vaccines. Regulatory officials need to be more open and transparent with vaccine producers and stake holders about how to obtain approval. However, even without approval, WHO has supported intradermal vaccination for decades.⁹ Broader use of the new shortened regimen beyond the clinical study stage might convince more public health agencies in low

and middle-income countries in Africa, Asia, and the Americas to reconsider use of intradermal vaccination for human rabies prevention. Enhanced post-marketing surveillance and development of an adverse event reporting system for vaccines might also help to weigh-up any disadvantages associated with local reactions or patient non-compliance with the advantages of greater product availability and cost savings to exposed patients.

Available and future needleless options for vaccine delivery broaden the overall scope of rabies immunisation in a wider One Health context.⁸⁻¹⁰ Given the ambitious timeline to eliminate dog-mediated human rabies globally by 2030, just over a decade is available to make this concept a reality. Encouraging research, such as that by Cantaert and colleagues,¹ helps to advance this goal.

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