

## Elimination of dog-mediated human rabies: scientific tools, One Health and partnerships

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### Summary

A world free of dog-mediated human rabies by 2030 would be an outstanding achievement. This ambitious goal for a neglected tropical disease, set by the World Organisation for Animal Health (WOAH), the World Health Organization, the Food and Agriculture Organization of the United Nations and the Global Alliance for Rabies Control together with partners and countries, has a clear and achievable pathway to success. In the 100 years since the inception of WOA, many scientific tools have been developed to support the elimination of dog-mediated rabies. In addition to these tools, engaging communities and health workers to build awareness to prevent bite exposures, managing dog populations and ensuring herd immunity through dog vaccination are key to achieving the elimination goals. The provision of post-exposure prophylaxis and care for exposed victims are important interventions on the human side. Success in eradicating rabies will require applying a One Health approach, an integrative and systemic approach to health grounded in the understanding that human health is closely linked to animal and environmental health. Political commitment and availability of adequate resources are key to achieving the Zero by 2030 goal.

### Keywords

Dog-mediated rabies – Elimination – Immunoglobulin – Neglected tropical diseases – One Health – Prevention – Vaccines.

## Introduction

Exposure to rabid dogs remains the major source of human rabies in Asia and Africa, responsible for the majority of the 55,000 cases of rabies estimated to occur annually [1]. The Zero by 30 rabies strategy aims to stop human rabies deaths by prioritising the disease reservoir in dogs as well as aligning rabies response to strengthening both veterinary and human health systems [2]. The elimination of dog-mediated rabies from North America and a number of countries in South America, as well as of dog- and wildlife-mediated rabies from Europe, through intensive vaccine programmes targeting animal reservoirs is testament to the value of promoting animal vaccination as the key strategic intervention for rabies elimination [3]. Similarly, a well-resourced research programme on dog vaccination demonstrated a 93% reduction in animal cases in KwaZulu Natal, a rabies-endemic area in South Africa, and an almost two-year cessation of human cases [4]. Dogs, however, remain of low economic importance, and Veterinary Services, which are limited in many low- and middle-income countries (LMICs), especially in rural areas, need to be significantly strengthened to achieve and maintain any gains. While dog vaccination ensuring a vaccine coverage of 70% is considered the most cost-effective and strategic intervention, much has still to be learnt about the dynamics of dog population control and different vaccine strategies [5].

Veterinary Services and veterinary resources are frequently diverted to respond to diseases of economic importance, especially when there are outbreaks and epizootics. The 2020–2023 Covid-19 pandemic led to major disruptions in dog vaccination campaigns as well as in administration of post-exposure prophylaxis, resulting in a record number of both dog and human rabies cases in several endemic areas [6]. The establishment of the World Organisation for Animal Health (WOAH) vaccine bank has enabled countries with limited resources to access valuable high-quality vaccines, but ensuring the provision of motivated and well-trained human resources and building public awareness of the value of anti-rabies vaccination campaigns remain challenges.

### From the past...

Rabies ranks among the most lethal infectious diseases, with essentially no effective options for treating either animals or humans with rabies disease, despite some valiant attempts to improve outcomes in infected humans. It has been almost 140 years since Louis Pasteur injected a nine-year-old boy with a crude rabbit-origin vaccine, the first recorded use of a rabies vaccine in a human victim. This has paved the way for post-exposure rabies prevention in humans using nerve tissue vaccines, leading in turn to the

production and use of safer and highly immunogenic killed cell culture-derived vaccines. Understanding of the pathogenesis of rabies has further enhanced understanding of the role of preventive therapy in humans. The cost of rabies vaccines and rabies immunoglobulin, limited availability of quality biologicals, especially immunoglobulin, complex regimens and the need for ensuring the cold chain are major barriers in many parts of Asia and Africa. World Health Organization guidelines published in 2018 [7] for the prevention of rabies in humans were developed using the best available scientific information and recommend pre- and post-exposure regimens using the intradermal administration of vaccines as a dose and cost-sparing strategy. This route of administration is highly effective and has long been adopted in Asia but is used on only a limited scale in Africa [8]. Community-centred programmes must be at the heart of rabies elimination programmes. Responsible animal ownership as well as awareness of the risks of rabies to communities and the value of dog vaccination are critical. Communities need to be informed of the importance of local wound care after animal exposure, especially where access to medical care is severely limited.

The tools to eliminate dog-mediated rabies in humans exist, but their implementation is still far from satisfactory. There are resource gaps for both human and dog rabies vaccines. The highly successful WOAHA-supported vaccine banks need to be expanded. Funding to support the supply of human biologicals for rabies prevention is critical, and the proposed Gavi initiatives are highly anticipated [9,10]. Accurately measuring burden of disease and success of interventions in order to promote continued interest in and funding for rabies control programmes is essential. The current lack of veterinary and human health laboratories to confirm cases is a significant limitation, especially in LMICs. The development of new scientific tools for surveillance and diagnosis that are sensitive, robust and affordable and can be used in the field is a priority.

### **...to the future**

Genomic surveillance needs to be expanded to inform rabies epidemiology and interventions and is particularly valuable during the end game, when the disease can circulate for extended periods at low levels in dog populations. Genetic characterisation is critical in identifying reservoirs responsible for ongoing endemic transmission, identifying spillover events and informing interventions [11]. Genomic surveillance is important to identify emerging lyssaviruses and inform their epidemiology. Molecular surveillance provides rich epidemiological information to identify transmission cycles within a given geographical area. This information can be used to strategise control

programmes and, importantly, elimination programmes, particularly in identifying cross-border spread.

Heat-stable, longer-acting vaccines are a priority on the animal side, as is consideration for expanding use of oral vaccines where appropriate. Research on and development of heat-stable human vaccines, ideally as single-dose regimens, need to be promoted. While the development of monoclonal antibodies to replace rabies immunoglobulin is welcomed, further scientific studies are required to confirm their effectiveness in different geographical settings [12].

## Conclusions

Elimination of dog-mediated rabies in humans is an achievable goal, building on the successes achieved and tools developed over the past 100 years. Rabies offers the best example of how goals can be reached and lives saved using a One Health approach. Successes can be built on to lead the way forward for the elimination of other neglected zoonotic diseases.

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