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A call to accelerate an end to human rabies deaths

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Introduction

Every year, an estimated 59 000 vaccine-preventable deaths occur globally due to rabies.¹ These deaths occur despite more than 100 years of existence of effective vaccines against rabies in humans and dogs, which serve as the main source of infection for humans.^{2,3}

Most of these deaths are in Africa and Asia among neglected populations that are hard to reach or economically disadvantaged, living in areas where availability of and access to these life-saving human rabies vaccines is poor and dog vaccination is low. Several epidemiological characteristics support the feasibility of rabies elimination. For example, the virus is transmitted by a known and accessible vector (ie, the domestic dog); transmission is by symptomatic animals, making it possible to identify suspected rabid animals; efficacious rabies vaccines exist that confer long-term immunity; and, across many settings, the basic reproduction ratio for rabies cases is low ($R_0 < 2$), with vaccination covering 70% of dogs in a region being sufficient to eliminate the disease.³⁻⁵

A global strategy

Using the complementary strategies of mass dog vaccination and prompt provision of rabies post-exposure prophylaxis vaccines to humans, many middle-income and high-income countries (eg, the USA, countries in western Europe, parts of Latin America, and parts of Asia, such as Japan and Malaysia) have successfully eliminated rabies disease as a public health problem.⁶ Supported by this success and epidemiological characteristics that make the virus possible to eliminate, and in response to the absence of a global coordinated strategy against dog-mediated rabies, WHO, the Food and Agricultural Organization of the UN, the World Organization for Animal Health, and the Global Alliance for Rabies Control endorsed a global framework for the elimination of human rabies by 2030 in all countries endemic for dog-mediated human rabies (ie, approximately 150 countries).^{7,8}

Besides ending preventable deaths due to rabies, in line with the UN Sustainable Development Goals, the framework for the Zero by 30 plan⁷ makes the case that rabies elimination supports health-system strengthening by improving access to health care, the mechanisms for surveillance of other infectious diseases, and the One Health approach, which supports collaboration between human and veterinary sectors and efficient use of the finite resources available to address public health challenges.

Barriers to progress

Despite these global frameworks, and with only 7 years to the 2030 target, progress towards rabies elimination

in many of the 150 countries that are still endemic for rabies is slow or non-existent. Only a few places, such as Goa, India, have reported elimination since the introduction of the global framework.⁹ The slow progress has been partly attributed to disruptions to mass dog vaccinations and access to post-exposure rabies vaccines associated with the COVID-19 pandemic.^{10,11} Similar effects have been estimated for other elimination programmes for neglected tropical diseases.¹² Progress in the elimination of neglected tropical diseases is also slowed by low prioritisation among the many other infectious diseases competing for resources and specialist expertise, insufficient financial and personnel resources for activities that support elimination programmes, and weak health-care systems that are unable to provide appropriate interventions in a timely manner to all people who are affected.

Translation of these global frameworks and targets into sustained investments in national rabies control programmes in most endemic countries is poor. Few countries have implemented comprehensive national control strategies comprising mass dog vaccination, integrated bite case management, affordable access to rabies post-exposure prophylaxis, and comprehensive disease monitoring and surveillance in both humans and animals.¹³

For vaccination campaigns of dogs to be sufficient to interrupt rabies transmission, vaccination coverage in all dog-owning communities should reach 70% of susceptible dogs, and vaccinations should be completed at least annually to maintain herd immunity.¹⁴ The gross underfunding of veterinary sectors in rabies-endemic countries impedes elimination activities, including through the poor availability and delivery of dog vaccines, leading to rabies persistence. Additionally, the population sizes of dogs in many rabies-endemic countries are uncertain, making planning of vaccination campaigns and establishing vaccination coverage challenging. In some parts of Africa, Asia, and South America, there are many roaming and stray dogs and no clear and well funded dog management plans, further complicating rabies elimination activities.^{5,15}

Access to rabies post-exposure prophylaxis vaccines for people with dog bites in these rabies-endemic countries is hindered by several factors. For example, the high cost of the vaccine, which is largely borne by patients; frequent stockouts of the vaccine at health facilities; inadequate demand forecasting and supply distribution systems for rabies vaccines in the health-care system, which are often separate from those used for routine childhood vaccines; people with dog bites not completing the vaccine course; and low awareness among community

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members and health-care workers on appropriate post-exposure treatment.^{16–18}

Gavi, the Vaccine Alliance, catalysing an end to rabies deaths

Gavi, the Vaccine Alliance, has helped to close the vaccine equity gap between low-income and high-income countries by making many vaccines accessible and affordable, increasing immunisation rates in low-income countries, expanding the scope of diseases covered at an accelerated pace, and strengthening health systems.¹⁹ Over the past two decades, Gavi innovations have enabled immunisation of nearly 1 billion children and prevented more than 16 million deaths.²⁰

During the 2008 and 2013 decisions of the Gavi 5-year vaccine investment strategies, rabies vaccines were considered but not taken up by Gavi. Instead, Gavi recommended modelling the economic and health impact of providing rabies post-exposure prophylaxis vaccines and assessing the manufacturing capacity, availability of logistics, such as cold chain, and health-system capacity to administer rabies post-exposure prophylaxis to people with dog bites. The results from these studies led to Gavi's decision in 2018 to include human rabies post-exposure prophylaxis in its 2021–25 vaccine investment strategy. The studies showed that a Gavi investment in the roll-out of rabies post-exposure prophylaxis would prevent an additional 489 000 deaths between 2020 and 2035, with the status quo resulting in an additional 1 million human lives lost due to rabies over the same period.²¹ Gavi's investment will be a major contribution to saving lives; spur the end of neglect, inaction, and deaths from rabies; and contribute to strengthening of health systems in three main ways.

Firstly, the Gavi investment will remove the key barriers to rabies prevention: the high cost of the vaccine and the scarce supply and availability globally and locally. In rabies-endemic countries, the unsubsidised cost of the full dose of rabies post-exposure prophylaxis can be up to US\$100. This cost places a notable financial burden on patients, especially in low-income settings, where most underserved communities living under the international poverty line of \$2·15 daily income reside. A Gavi investment would remove this personal expenditure and make these life-saving vaccines accessible. Rabies post-exposure prophylaxis is an on-demand and expensive government expenditure within the health-care system. As a result, the vaccine is seldom stocked in all health facilities and is frequently out of stock in the designated health facilities.^{16,17} Considering the current global supplies for rabies post-exposure prophylaxis, increased rabies post-exposure prophylaxis provision with a switch to the dose-sparing abridged 1-week intradermal regimen would be feasible, increasing rabies post-exposure prophylaxis accessibility

and availability to people who are at high risk of exposure to rabies.^{21,22}

Secondly, a Gavi investment in rabies post-exposure prophylaxis will catalyse dog vaccination campaigns. Modelling studies showed that scaling up mass dog vaccination could eliminate dog-mediated rabies by the 2030 target, with provision of rabies post-exposure prophylaxis being cost-effective when combined with risk assessments that promote judicious use of these human vaccines.^{21,23} To reach elimination and reduce the need for rabies post-exposure prophylaxis vaccines, countries should invest in mass dog vaccinations to stop transmission in the reservoir species. A Gavi investment in rabies post-exposure prophylaxis could be linked to dog vaccinations to ensure that countries roll out the two complementary strategies together.

Thirdly, a Gavi investment will strengthen health systems, including promoting the One Health approach to dealing with public health threats. Rabies is a quintessential One Health disease, with the two main strategies for its elimination requiring close collaboration between human and veterinary sectors. A Gavi investment would be more than a sum of its parts, as its announcement in 2018 has already stimulated the veterinary sector and improved surveillance in some countries. Today, most emerging public health threats are zoonotic. The responses to these threats (eg, contact tracing and recommended public health measures) require community engagement. Rabies-elimination activities are ideal for strengthening One Health structures that close the equity gap; for example, rabies post-exposure prophylaxis vaccines reaching all people at high risk of exposure to rabies without the barriers of cost, availability, and access, and veterinary services and surveillance reaching animal populations to promptly detect and respond to threats of zoonotic diseases, preventing future pandemics.

New tools, technologies, and approaches

Most of the success stories on rabies elimination in high-income countries were mainly driven by veterinary public health. In low-income countries, the scarcity of veterinary personnel and insufficient financing of disease surveillance, prevention, and control should be urgently addressed, and innovations and new tools that increase the speed and efficiency of progress towards rabies elimination should be adopted. Several promising tools, technologies, and approaches exist that might accelerate time to elimination, including data-driven approaches to dog vaccinations,²⁴ short rabies post-exposure prophylaxis regimens and potential use of pre-exposure prophylaxis in highly endemic settings,^{25,26} improved diagnostics through validated rapid kits,²⁷ integrated bite case management approaches to risk management and use of rabies post-exposure prophylaxis,^{23,28} regional provision of quality dog vaccines through the World Organization for

Animal Health rabies vaccine banks,²⁹ and use of oral rabies vaccines to improve vaccination coverage, especially in areas with many roaming dogs.³⁰ Many of these tools, technologies, and approaches require further evaluation before scaling up but present opportunities to improve delivery of interventions and measurement of elimination progress. One of the focus areas of the United Against Rabies forum (supported by WHO, the Food and Agricultural Organization of the UN, and the World Organization for Animal Health) is “Effective use of vaccines, medicines, tools and technologies”, and the forum has a role in evaluating these resources and supporting scale-up activities.³¹

A call to action

At the time of writing, the Gavi position on implementing its commitment is unclear, with a risk that a decision could be delayed until at least 2024. This delay does not only scupper any chance of achieving the 2030 goal but also risks emphasising the global inequities in health. Gavi has the opportunity to be a leader in improving access to rabies post-exposure prophylaxis and ending preventable deaths from rabies, strengthening health systems that support emergency supply chains (eg, for rabies post-exposure prophylaxis and snake antivenom), and operationalising the One Health systems, for which the benefit goes beyond controlling endemic diseases, such as rabies, to addressing other diseases, including those that are prone to outbreaks, epidemics, or pandemics.³¹ If Gavi fails to meet the vaccine investment strategy commitments by 2022 and instead delays until 2024, then the 2030 target of ending rabies will be missed, and more than 40 000 rabies deaths will occur that would have otherwise been prevented.

Contributors

All authors contributed to the conceptualisation and writing of this Viewpoint.

Declaration of interests

We declare no competing interests.

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