

# Infectious Disease Prevention, Control, Elimination (and Eradication?!) Terminology: Applications to Lyssaviruses

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## Abbreviations

NTD: Neglected Tropical Diseases; PEP: Postexposure Prophylaxis; Prep: Preexposure Prophylaxis; RABV: Rabies Virus

“Words have no power to impress the mind without the exquisite horror of their reality.” -Edgar Allan Poe

What is in a word? During these challenging ‘pandemic fatigue’ times, seemingly technical words are often bandied about along a spectrum of ideas from control to elimination of SARS-CoV-2. These conversations have ramifications beyond emerging coronaviruses, particularly among neglected tropical diseases (NTD) and their 21<sup>st</sup> century fate. Rampant confusion is understandable, among professionals and the public alike, as biomedical terms are often used interchangeably, and definitions abound. Review of some applied public health terminology [1-4] is useful for a cogent discussion of several basic concepts relevant to present global goals on NTD: prevention (i.e., procedures to stop, hinder, or avoid the manifestation of a disease; histoplasmosis prevention); control (i.e., reduction of disease incidence, prevalence, morbidity, or mortality to a locally acceptable level as a result of deliberate efforts, with continued intervention measures required to maintain the reduction; flea control); elimination (i.e., reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts; poliomyelitis elimination from the Americas); eradication (i.e., permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; smallpox and rinderpest eradication); and extinction (i.e., total removal from nature and the laboratory; no directed infectious disease examples yet, but a multitude of organismal extinctions throughout the history of life on earth).

All of these terms may be taken out of context and be difficult to place into daily practice, particularly, when dealing with zoonotic NTD. Rabies, an acute, progressive viral encephalitis, serves as a model for such considerations [5]. Hosts include warm-blooded vertebrates, and all mammals are susceptible, with major reservoir representatives among the Carnivora and Chiroptera [6]. Often forgotten, rabies is a vaccine-preventable disease, either by timely administration of postexposure prophylaxis (PEP) to those bitten by rabid animals or applied as preexposure prophylaxis (PrEP) to individuals at risk of exposures (e.g., animal control workers, cavers, diagnostic staff, veterinarians, etc.), as well as domestic animals, in an obvious One Health application [7]. Despite a century of sensitive and specific diagnostic tests, practical epidemiological and pathobiological insights, and safe and effective vaccines, most developing countries remain in a reactive control mode for affected animal and human communities, as with other NTD in a cycle of poverty.

Rabies is global in distribution, although apparently never have been reported in some localities (e.g., New Zealand, Virgin Islands, etc.), such as in many parts of Oceania [8]. Such splendid isolation minimizes the threat of introduction, together with importation safeguards. However, these measures do not remove the risk of an incursion, as seen historically with canine rabies introduction to Guam or

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even the untoward discovery of a rabid bat to Hawaii, captured in a transport container [9,10]. Some countries (e.g., Malta, Japan, etc.) were able to eliminate the disease. Several other locales believed ‘rabies-free’ during the 20<sup>th</sup> century (e.g., Australia, Taiwan, the United Kingdom, etc.) are now recognized as enzootic, with wildlife lyssaviruses [7,8]. Clearly, rabies is not a candidate for eradication [5,7,11]. Factors include: the broad spectrum of hosts; the hundreds of millions of individuals that may comprise some populations of mammalian species; the inaccessibility of some taxa; the limitations of laboratory-based surveillance in many countries; the ongoing need for pathogen discovery; the lack of efficacious biologics against antigenically diverse lyssavirus species; etc.

Misunderstanding of such terms may result in serious health and economic consequences. For example, there is a global plan for the elimination of human rabies caused from dogs by 2030 [12,13]. Most human rabies cases are caused via dog bites, and regional progress in the Americas and Europe demonstrate the feasibility for success in developing countries [7,12-14]. However, such a distinction among selective rabies virus (RABV) variants does not mean rabies has truly been eliminated from any of these regions [7,11,15]. Conceptual confusion or trivialization regarding an ancient pariah such as rabies, known for the most extreme case fatality of any infectious disease, could result in death, or years of reactive control from a new incursion. As a case in point, even highly developed countries, such as the USA, are endemic for rabies, now perpetuated by wildlife [16]. During 2021, at least five human cases were reported, the most in a decade [17,18]. One patient acquired infection with canine RABV during a visit to the Philippines. The other four fatalities were due to bat RABV: one patient from Illinois refused PEP after being bitten by a rabid bat; patients in Texas and Idaho may not have realized they were exposed by bats; and the death of a Minnesota man occurred despite receiving PEP, a rare and unusual episode [17,18]. These cases demonstrate the difficulties of rabies prevention, control, and elimination, especially due to the reality of domestic animal wildlife rabies, and raise the specter of the unintended consequences that the COVID-19 pandemic may play in the limitations of public health communications, education and intervention [19,20]. In closing, disease prevention, control ‘... elimination and eradication programs are laudable goals, but they carry with them an awesome responsibility ...’, even in non-pandemic times [1]. This is applicable across the microbiological spectrum and our choice of management terminology matters.

### Conflict of Interest

None.

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