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Survival in human rabies: What conventional medicine has achieved and what homeopathy claims: A critical narrative review

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Abstract

Human rabies is classically described as an almost invariably fatal viral encephalitis caused by viruses of the genus *Lyssavirus*, transmitted mainly through bites from infected dogs and bats. It is estimated to cause about 59,000 human deaths per year in more than 150 countries, with over 95% of deaths occurring in Africa and Asia, and case-fatality after onset of clinical symptoms remains close to 100% [1, 2]. Prevention through Post-Exposure Prophylaxis (PEP), including vigorous wound cleansing, vaccination with cell-culture vaccines and rabies immunoglobulin in severe exposures, is highly effective and explains why clinical rabies is now considered largely a failure of prevention [1, 3, 6].

Despite this, in recent decades sporadic reports have described survivors after symptom onset, generally associated with Intensive Care Unit (ICU) management, such as the celebrated case treated with the “Milwaukee protocol” in 2005 and subsequent experiences, including the Recife protocol in Brazil [9-12]. Recent reviews emphasize, however, that the number of well-documented survivors remains extremely low, that most attempts using the Milwaukee protocol have failed, and that survival appears to depend primarily on host factors (such as early development of neutralizing antibodies) and the quality of intensive care rather than on any specific pharmacological regimen. [4, 11-13]

In parallel, the classical homeopathic literature has, since the nineteenth century, described the use of *Lyssinum* (*Hydrophobinum*)-a nosode prepared from rabid dog saliva in cases of “hydrophobia”, including the 1881 report by Berridge [17]. However, these texts lack laboratory confirmation, modern clinical criteria and systematic documentation of evolution and outcomes. *Materia medica* texts such as Boericke’s simply list symptoms and proposed indications for *Lyssinum*, without presenting clinical trials, case series or any robust evidence of efficacy in the prevention or treatment of rabies. In this article, we review the available evidence on survival in human rabies treated according to intensive conventional medical protocols, with emphasis on the Milwaukee and Recife protocols, and contrast these data with what is actually found in the homeopathic literature and in reviews on traditional medicine. We also propose two tables summarizing, in chronological and synthetic form, the main documented treatment milestones in conventional medicine and the type of evidence available in homeopathy and traditional practices.

Keywords: *Lyssinum*, *Hydrophobinum*, Milwaukee protocol, Recife protocol, human rabies, *lyssavirus* encephalitis, intensive care, traditional medicine, homeopathy

Introduction

Rabies is an acute encephalitis that is almost always fatal, caused by viruses of the genus *Lyssavirus* (family *Rhabdoviridae*) that infect domestic and wild mammals and are transmitted to humans mainly by bites of infected animals, particularly dogs and bats [1, 3, 7]. The World Health Organization (WHO) estimates that rabies causes approximately 59,000 human deaths per year, most of them in poor rural areas of low- and middle-income countries [1, 2]. A global modelling study by Hampson *et al.* calculated that endemic canine rabies accounts for about 59,000 deaths annually, 3.7 million DALYs and economic losses in the order of 8.6 billion US dollars per year [2].

Clinically and neuropathologically, rabies is characterized by a variable incubation period, a nonspecific prodrome and a subsequent encephalitic phase, which may present as the “furious” form (with hydrophobia, aerophobia, hyperexcitability and dysautonomia) or as a paralytic form often mistaken for Guillain-Barré syndrome or myelitis [3, 7].

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Neuropathological studies show that, rather than extensive neuronal necrosis, there is axonal injury, mitochondrial dysfunction, oxidative stress and impairment of specific neuronal circuits, which contribute to the clinical picture and fatal outcome [3, 4].

Post-Exposure Prophylaxis (PEP) based on thorough wound washing with soap and water, modern cell-culture vaccines and rabies immunoglobulin according to exposure category is highly effective when implemented correctly and early. [1, 5, 6] International and national guidelines emphasize that clinical human rabies should, in practice, be regarded as a “failure of the prevention system”, whether due to lack of risk awareness, delay in seeking care, poor access to PEP or interruption of the vaccination schedule [5-7].

In Brazil, a recent analysis of two decades of human cases between 2001 and 2025 identified 188 reported cases, with a mean of 7.5 cases per year, predominance in the North and Northeast regions, and progressive shift in the main source of infection from dogs to haematophagous bats, with participation of non-human primates in some outbreaks [8]. The vast majority of patients died, despite attempts at intensive management in selected cases [8, 9, 11].

Historically, reports of survival after onset of clinical symptoms are exceptional. Comprehensive reviews on the management of human rabies, published before the era of aggressive protocols, already stressed that the disease is “almost invariably fatal” and that any therapeutic strategy should be viewed critically, with emphasis on prevention and palliative care [4, 7, 9]. From 2005 onwards, with the report of a teenage survivor treated with an induced coma regimen in the United States, the so-called Milwaukee protocol emerged, prompting a series of subsequent attempts, including Brazilian adaptations such as the Recife protocol [9-12]. In parallel, non-conventional therapeutic traditions including traditional medicine and homeopathy have maintained narratives of supposed “treatments” for rabies, often without diagnostic confirmation or systematic documentation [14-18].

This article examines what is currently known about clinically manifest human rabies treated with intensive conventional approaches, how many and which survivors are reasonably documented, and how this evidence compares with classical homeopathic reports and reviews on traditional medicine.

Overview of conventional medicine: prevention and the therapeutic challenge

The cornerstone of human rabies control is prevention. The WHO and other international bodies recommend mass dog vaccination campaigns, community education, improved access to PEP and, in some settings, pre-exposure vaccination for high-risk groups [1, 5, 6]. The 2018 WHO position paper on rabies vaccines updated pre- and post-exposure regimens, introducing abbreviated intradermal schedules with good immunogenicity and lower cost [5, 6]. Despite these advances, implementation failures persist, particularly in rural areas and in countries with fragile health systems [1, 2].

From a clinical standpoint, classic management guidelines emphasize that once neurological signs are established, rabies should be considered practically irreversible, with the focus on diagnostic confirmation, symptomatic control (pain, agitation, seizures, secretions) and humane support for patients and families [4, 7, 13]. Since the 1970s there have

been isolated attempts at intensive management, such as the experience of Gode *et al.* in India, in which patients with rabies received intensive care and treatment of complications, with reports of temporary stabilization but no evidence of sustained cure [9].

Neuropathogenic reviews highlight that lyssavirus infection disrupts neuronal circuits in a diffuse manner, with axonal injury and mitochondrial dysfunction, and that to date no antiviral agent has shown consistent efficacy in animal models or in humans [3, 4]. Thus, the challenge of specific therapy remains unresolved, and any report of survival should be interpreted cautiously, taking into account host factors (such as prior vaccination), timing of diagnosis, availability of intensive care and diagnostic criteria used. [4, 7, 12].

Intensive treatment protocols: Milwaukee, Recife and other experiences

From supportive care to the Milwaukee protocol

Until the early 2000s, management of human rabies consisted essentially of supportive treatment, symptomatic control and palliative care [4, 7, 13]. In 2005, Willoughby *et al.* published the case of a 15-year-old girl in the United States who developed rabies after a bat bite, without prior PEP, and was treated with a protocol that included induced coma with deep sedation, ketamine, midazolam, amantadine, ribavirin and advanced intensive care [10, 11]. The patient survived and achieved gradual neurological recovery during follow-up, and the regimen became known as the Milwaukee protocol.

Initial enthusiasm led to attempts to replicate the protocol in several countries. A systematic review by Ledesma *et al.*, which evaluated the use of the Milwaukee and Recife protocols between 2004 and 2019, identified dozens of cases in which elements of these strategies were applied, but found that most patients died, making it difficult to estimate any true efficacy [11]. More recent analyses, such as the review by De Pijper *et al.*, reinforce that the few well-documented survivors shared factors such as early development of neutralizing antibodies in serum and cerebrospinal fluid, relatively early diagnosis and access to well-resourced ICUs, rather than a particular drug combination [12].

Jackson and colleagues argue, based on case series and extensive review, that two decades of attempts have failed to demonstrate reproducible efficacy of the Milwaukee protocol and that it may, in fact, have diverted attention from more rational therapeutic approaches grounded in disease pathophysiology and high-quality intensive care [4, 13]. These authors contend that the truly plausible component of the Milwaukee protocol is intensive supportive care itself, which had already been implemented since the first survival report in 1972, and that there is no robust evidence supporting the proposed drug combination. [4, 9, 10, 13].

Brazilian adaptation: the Recife protocol

In Brazil, the Ministry of Health published in 2009 the “Protocol for the treatment of human rabies in Brazil”, known as the Recife protocol, which adapted the Milwaukee experience to the reality of Brazilian hospitals [7, 9, 11]. This protocol proposed a set of intensive measures, including deep sedation, judicious use of antivirals, immunoglobulin administration, advanced neurological and haemodynamic monitoring, and specific recommendations for gradual

withdrawal of sedation according to neutralizing antibody titres in cerebrospinal fluid rather than a fixed day-by-day schedule [9, 11].

The analysis by Ledesma *et al.* showed that both the Milwaukee and Recife protocols emphasize sedation, antivirals and haemodynamic support, but differ in aspects such as timing of sedation withdrawal, use of ancillary tests and criteria for selecting patients for aggressive therapy [11]. Recent epidemiological studies on human rabies in Brazil, such as the nationwide review by Catozo *et al.*, document few survivors associated with use of the Recife protocol, generally in young patients, infected by bats, with relatively early diagnosis and some form of prior immunization [8, 9, 11]. Even so, the total number of survivors remains extremely small compared with the overall number of clinical cases [8, 11, 12].

Recent reviews and current situation

The review by De Pijper *et al.*, published in 2025, synthesizes recent experience in two patients treated intensively in the Netherlands and systematically revisits the literature on survivors of human rabies [12]. The authors emphasise that, based on well-documented cases, survival with functional recovery is possible but rare and depends on a combination of factors: early suspicion, rapid diagnostic confirmation, development of neutralizing antibodies, competent intensive care and, possibly, lower initial viral inoculum [3, 4, 12].

Contemporary reviews on human rabies therapy underscore that there is still no specific antiviral with proven efficacy in humans and that priorities should be strengthening prevention, timely diagnosis and high-quality palliative care [4, 7, 13]. Warrell *et al.* explicitly proposed the concept of an “imperative of palliation” in rabies encephalomyelitis, arguing that only a minority of patients fulfil clinical, epidemiological and structural criteria for attempts at aggressive management, whereas most benefit more from compassionate and adequate palliative care [13].

In summary, conventional medicine currently documents a small number of human rabies survivors, typically in settings of advanced intensive care, without allowing the favourable outcome to be attributed to any single pharmacological protocol. The central message of guidelines remains that clinical rabies is still, in practice, almost invariably fatal, and the priority should be prevention, PEP and equitable access to these measures [1, 2, 4-7].

Traditional medicine and homeopathy in rabies: what the literature actually shows

Although PEP based on modern vaccines and rabies immunoglobulin is highly effective, in many contexts exposed individuals initially turn to traditional medicine and healers, for cultural reasons, issues of access or trust in health institutions. A review by Beasley *et al.* analysed the role of traditional medicine and healers in rabies prevention and showed that a significant proportion of bitten individuals, in several countries, first seek traditional treatments before receiving PEP (or instead of it), contributing to delays and failures in prophylaxis [14].

A meta-analysis by Asres *et al.* on the use of traditional medicine among people exposed to rabies in Ethiopia found very high prevalences of reliance on traditional healers and herbal preparations, frequently associated with non-use or

interruption of PEP schedules and, consequently, increased risk of progression to clinical rabies [15]. Anthropological studies in communities where “rabies is not seen as a disease” but as a consequence of spiritual imbalance or divine punishment reinforce the role of local beliefs in the decision to seek or not seek biomedical care [16].

It is important to note that these studies do not document cure of clinical rabies by traditional medicine, but rather the high frequency of its use in exposures potentially at risk, before symptom onset [14-16]. The “apparent effectiveness” reported by healers derives largely from the low absolute probability of progression to rabies after many bites especially in areas where some dogs may be vaccinated and not from intrinsic efficacy of traditional treatments [2, 14, 15].

In the specific field of homeopathy, the classical literature describes Lyssinum (also called Hydrophobinum) as a nosode prepared from rabid dog saliva, potentised according to homeopathic principles [17, 18]. Materia medica texts, such as Boericke’s, list a series of symptoms considered indicative of Lyssinum, based on provings and anecdotal reports, including extreme irritability, fear, hypersensitivity to stimuli, salivation and images of hydrophobia [18].

The paper by Berridge, published in 1881 in the *Homoeopathic Physician*, entitled “Lyssin in hydrophobia; euthanasia from the simillimum”, discusses a case of “hydrophobia” treated with Lyssinum, with emphasis more on a “good death” and subjective symptom relief than on objective cure of infection [17]. This and other reports from that era lack essential components of modern diagnosis: no laboratory confirmation, incomplete clinical description of classic rabies signs, absence of long-term follow-up, and no independent documentation [3, 4, 17].

To date, there are no randomized clinical trials, well-documented case series or modern case reports with laboratory confirmation that demonstrate efficacy of Lyssinum or any other homeopathic medicine in the prevention or treatment of clinical human rabies. Recent reviews on traditional medicine explicitly state that there is no evidence that alternative practices, including homeopathy, reduce mortality once rabies symptoms have started [14-16].

From an evidence-based medicine standpoint, Lyssinum therefore remains a nosode described in homeopathic materia medica and historical reports, without demonstration of therapeutic efficacy in human rabies. The contrast with conventional PEP is striking: while PEP exhibits well-established effectiveness in observational and modelling studies, the use of Lyssinum rests solely on homeopathic doctrine and nineteenth-century anecdotal reports [1, 2, 5, 14-18].

Critical comparison between conventional medicine and homeopathy in rabies

The comparison between conventional and homeopathic approaches to human rabies reveals two completely different realities. In conventional medicine, the foundations of control are well defined: dog vaccination, early and appropriate PEP, surveillance, health education and, in selected cases of clinical rabies, intensive care unit management [1, 2, 4-8, 11, 12]. Although survival after symptom onset is rare, it is documented in a small but growing number of cases, with detailed descriptions of clinical signs, laboratory tests, antibody titres, therapeutic interventions and outcomes [9-12].

The recent literature indicates that even among patients treated with aggressive protocols, case-fatality remains very high and there is no convincing evidence that the Milwaukee protocol, as a pharmacological regimen, improves prognosis compared with high-quality intensive care [4, 11–13]. In contrast, well-structured palliative care is increasingly recognised as an essential part of management for most patients who are not candidates for aggressive therapies [13].

In homeopathy, by contrast, there are only historical reports and materia medica descriptions of *Lyssinum*, without modern diagnostic confirmation, documentation of sustained survival or comparative studies [17, 18]. As far as can be determined from indexed literature, no case series of clinical human rabies treated with *Lyssinum*, with laboratory confirmation and adequate follow-up, has been published. In terms of evidence-based medicine, this places *Lyssinum* in the realm of untested or refuted hypotheses, rather than established therapies [14–18].

Reviews on traditional medicine and the use of healers in rabies exposures further highlight an important public health point: in many settings, primary reliance on traditional practices delays or prevents access to effective PEP, increasing the risk of progression to clinical rabies [14, 15]. Ethically, there is no justification for replacing or postponing PEP based on vaccines and immunoglobulin with treatments whose efficacy is unproven, whether traditional or homeopathic.

Based on the available literature, it is therefore possible to state that: (1) clinical human rabies remains, in practice, almost always fatal; (2) the small but real number of well-documented survivors receiving intensive management appears to be more related to individual factors, early diagnosis and high-quality intensive care than to any specific pharmacological protocol such as the Milwaukee regimen; (3) there is no evidence of efficacy of homeopathy, and in particular of *Lyssinum*, in the prevention or treatment of human rabies; and (4) prioritising traditional or homeopathic practices at the expense of conventional PEP represents an additional and avoidable risk [1–18].

Conclusions

Human rabies remains an “almost 100% fatal” disease after onset of symptoms, despite considerable advances in understanding of pathogenesis and in the organisation of

intensive management protocols. Current evidence shows that survivors exist but are rare, and that their survival is more closely related to individual factors, early diagnosis and the quality of intensive care than to the application of any specific pharmacological protocol such as the Milwaukee regimen. The Brazilian experience with the Recife protocol illustrates an attempt to adapt aggressive strategies to local reality, with a few cases of survival but no substantial change in the overall picture of high mortality.

By contrast, the homeopathic literature on *Lyssinum* consists essentially of historical reports and materia medica doctrine, without modern documentation of efficacy. Contemporary reviews on traditional medicine and healing practices emphasize that such approaches have not been shown to reduce rabies mortality and may delay access to effective PEP.

From the standpoint of science and public health, priorities remain expanding access to post-exposure prophylaxis, strengthening animal and human vaccination programmes, improving epidemiological surveillance and ensuring high-quality palliative care for clinical rabies cases. Any discussion about the role of complementary or alternative approaches must acknowledge, transparently, the absence of robust evidence of efficacy and the risk of diverting patients from interventions with proven effectiveness.

Declarations

CRediT Authorship Contributions

J.F. de Carvalho, Conceptualization; Methodology; Formal Analysis; Investigation; Data Curation; Writing, Original Draft; Writing, Review & Editing; Visualization; Project Administration.

Conflict of Interest Statement

The author declares no conflicts of interest related to this work.

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Ethical Considerations

Ethical approval was not required because all data analyzed originated from previously published archaeological studies without involvement of living human participants.

Table 1: Main milestones and examples of human rabies treatment in conventional medicine (chronological summary, not exhaustive)

Year (approx.)	Setting / context	Main treatment strategy	Brief comment
1970–1976	India	Early attempts at intensive care (Gode <i>et al.</i>)	Temporary stabilization; no evidence of sustained cure. [9, 10]
2003	International reviews	Guidelines emphasize prevention and supportive care	Clinical rabies regarded as almost always fatal; focus on PEP and palliation. [4, 7]
2004–2005	USA (Milwaukee)	Milwaukee protocol with induced coma, antivirals and ICU	Survival of a 15-year-old girl; widely publicized index case. [10, 11]
2004–2018	Multiple countries	Multiple attempts to apply the Milwaukee protocol	Most patients died; lack of reproducible efficacy. [11–13]
2009	Brazil (Recife)	Publication of national protocol adapting Milwaukee	Recife protocol; sedation, antivirals, immunoglobulin, advanced monitoring. [9, 11]
2004–2019	Several countries (review)	Comparative assessment of Milwaukee and Recife	Ledesma <i>et al.</i> review 65 articles; a small minority of survivors; efficacy hard to estimate. [11]
2001–2025	Brazil (national series)	Surveillance, with selected cases on Recife protocol	188 human cases; very few survivors linked to specialized ICU treatment. [8, 9, 11]
2025	Netherlands (recent cases)	Individualised intensive ICU management (no single protocol)	De Pijper <i>et al.</i> report two intensively treated cases; review confirms rarity of survival. [12]

Table 2: Evidence on homeopathy, *Lyssinum* and traditional medicine in rabies (synthetic overview)

Period / source	Type of evidence	Main characteristics	Main limitations
19 th century (Berridge, 1881)	Case report in homeopathic journal	Discussion of “hydrophobia” treated with Lyssinum, focusing on symptom relief/euthanasia. ^[18]	No laboratory diagnosis; incomplete clinical description; outcome not clearly curative.
Homeopathic materia medica (Boericke)	Homeopathic doctrine / provings	Description of symptoms attributed to Lyssinum and theoretical indications for “hydrophobia”. ^[19]	No clinical trials or case series; purely doctrinal evidence.
Reviews on traditional medicine (Africa, Asia)	Narrative and systematic reviews	High use of healers and traditional preparations before PEP; delays in access to biomedical care. ^[14–16]	Do not document cure of clinical rabies; “successes” largely reflect low baseline progression rates.
Meta-analyses in rabies-exposed individuals (Ethiopia, etc.)	Systematic review and meta-analysis of traditional medicine use	High prevalence of traditional medicine use; association with lower PEP uptake and higher potential risk. ^[15]	Observational evidence; focus on care-seeking behaviour, not cure of clinical rabies.
Current situation (indexed literature)	Absence of modern clinical series with Lyssinum	No well-documented series of confirmed human rabies cases treated with Lyssinum with sustained survival. ^[14–18]	No basis to attribute any therapeutic efficacy to homeopathy in rabies based on available evidence.

Use of Artificial Intelligence

The author used ChatGPT in the linguistic revision, formatting adjustments, and technical editing of the manuscript. All intellectual content, data interpretation, scientific conclusions, and responsibility for the final version rest entirely with the author.

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