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Rabies Vaccine Failure Revisited: Integrity, Manufacturing Technologies, and Public Health Implications

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Abstract

Rabies is a universally fatal zoonotic disease once clinical signs appear, yet it is entirely preventable through timely vaccination and post-exposure prophylaxis. Modern cell-culture rabies vaccines have demonstrated high efficacy and safety over several decades. Recent international alerts regarding the circulation of falsified rabies vaccine batches have generated concern and have been widely reported as "rabies vaccine failure." This article critically examines the concept of rabies vaccine failure, differentiating true biological failure from pharmaceutical quality and supply-chain failures. In addition, current rabies vaccine production technologies, manufacturing processes, and quality control measures are reviewed. The implications of counterfeit vaccines for clinical practice, public trust, and regulatory systems are discussed. Evidence indicates that recent events reflect failures of product integrity rather than intrinsic limitations of rabies vaccine technology.

Keywords: Rabies, vaccine failure, Counterfeit vaccines, Rabies vaccine production, post-exposure prophylaxis, public health

Introduction

Rabies is an acute, progressive viral encephalitis caused by viruses of the genus *Lyssavirus* (family *Rhabdoviridae*). The disease is responsible for an estimated 59,000 human deaths annually, with the highest burden occurring in Asia and Africa [1]. Once neurological symptoms develop, rabies is almost invariably fatal, making prevention through vaccination and post-exposure prophylaxis (PEP) essential [2].

Cell-culture-derived rabies vaccines have been in use since the 1970s and have largely replaced older nerve-tissue vaccines due to superior safety and immunogenicity profiles [3]. Despite their proven effectiveness, recent international advisories regarding falsified rabies vaccines have raised concerns about vaccine effectiveness and have been widely interpreted as instances of "vaccine failure." This mischaracterization risks undermining public confidence in rabies immunization programs.

Recent Reports of Alleged Rabies Vaccine Failure

In late 2025, the Australian Technical Advisory Group on Immunisation (ATAGI) issued a health alert warning of counterfeit rabies vaccine batches circulating in India, particularly involving the product Abhayrab® [4]. Individuals vaccinated with these batches were advised to consider revaccination with verified WHO-approved vaccines.

The manufacturer, Indian Immunologicals Limited (IIL), later confirmed that one specific batch had been identified as counterfeit and withdrawn, emphasizing that the issue was not related to manufacturing failure of authentic vaccine lots [5]. These events highlight vulnerabilities in pharmaceutical supply chains rather than shortcomings of rabies vaccine science.

Biological Vaccine Failure

True vaccine failure refers to inadequate protection despite administration of a potent, authentic vaccine according to recommended schedules. In rabies, such failures are rare and are most often associated with the following causes i.e i) Delayed initiation of PEP, ii) Failure to administer rabies immunoglobulin (RIG) in category-III exposures, iii) Immunosuppression in the recipient, iv) Incorrect administration site or dosing schedule etc. Studies consistently demonstrate that WHO-approved rabies vaccines induce protective virus-neutralising antibody titres (≥0.5 IU/mL) in the vast majority of recipients [6].

Pharmaceutical Quality and Programmatic Failure

By contrast, counterfeit or substandard vaccines represent pharmaceutical quality failures, in which the administered product lacks adequate antigen content or potency. These failures may lead to false reassurance and delayed effective treatment, with potentially fatal consequences in rabies-exposed individuals.

Immunological Basis of Rabies Vaccination

Rabies virus enters peripheral nerves at the site of exposure and migrates centripetally to the central nervous system. Vaccination aims to elicit neutralising antibodies against the rabies virus glycoprotein (G protein), thereby preventing viral entry into host cells [7].

Protective immunity depends on: i) Antigenic integrity of the vaccine, ii) Adequate antigen dose, iii) Timely immune response prior to CNS invasion. This explains why vaccine authenticity and potency are critical determinants of clinical outcome.

Rabies Vaccine Production Technologies

Modern rabies vaccines are inactivated virus vaccines produced using cell-culture systems under Good Manufacturing Practice (GMP) conditions.

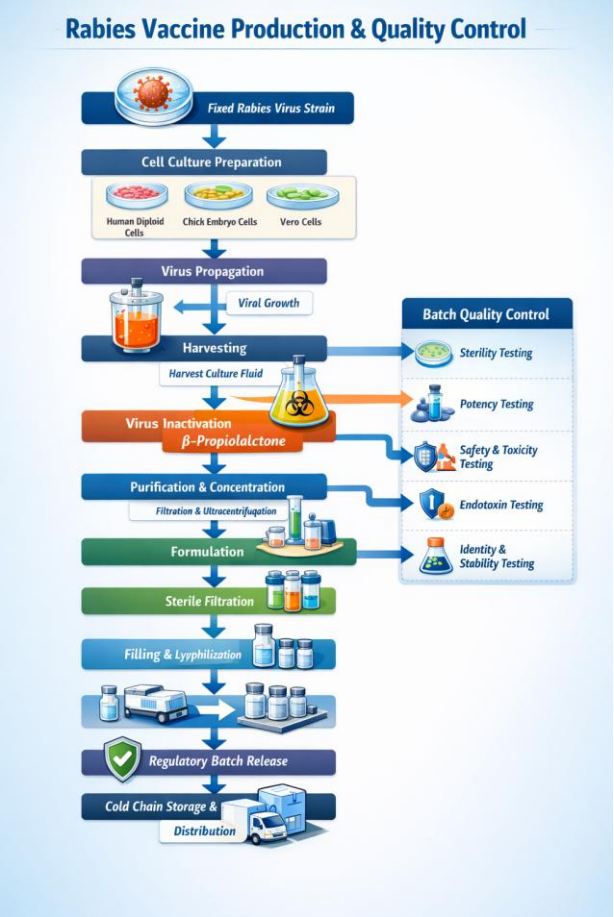

Figure 1: Overview of inactivated rabies vaccine production, highlighting key manufacturing steps and essential quality control measures ensuring safety, potency, and regulatory compliance.

1 Human Diploid Cell Vaccine (HDCV)

HDCVs are produced using human diploid fibroblast cell lines (e.g., MRC-5 or WI-38). These vaccines exhibit high immunogenicity and an excellent safety profile but are associated with higher production costs [8].

2 Purified Chick Embryo Cell Vaccine (PCECV)

PCECVs are produced by propagating rabies virus in primary chick embryo fibroblast cultures. They are widely used globally due to cost-effectiveness and strong immunogenicity [9].

3 Purified Vero Cell Rabies Vaccine (PVRV)

PVRVs are manufactured using continuous Vero cell lines and are highly scalable, making them suitable for mass immunization programs in endemic regions [10].

4 Emerging Vaccine Platforms

Novel platforms, including mRNA-based rabies vaccines, have demonstrated promising immunogenicity in preclinical and early clinical studies and may represent future alternatives to conventional vaccines [11].

Public Health Implications

The circulation of counterfeit rabies vaccines poses a serious public health threat, particularly in endemic regions. Misinterpretation of these events as vaccine failure risks increasing vaccine hesitancy and undermining rabies control programs. Strengthening regulatory oversight, pharmacovigilance, and public communication is essential to prevent similar incidents.

Conclusion

Recent reports of rabies vaccine-associated concerns reflect failures in product integrity and supply-chain governance rather than intrinsic limitations of rabies vaccine technology. Authentic, WHO-approved rabies vaccines produced using established cell-culture methods remain highly effective when administered correctly. Ensuring vaccine authenticity and regulatory vigilance is critical to sustaining progress toward global rabies elimination.

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