

Factors influencing the immunogenicity of rabies vaccines, evaluation of time effect over several decades: a literature review and meta-regression

Fernando Morelli¹, Christèle Augard¹, Laurent Coudeville¹, Catherine Bravo¹, Hervé Bourhy², Beatriz Quiambao³, Sergio Recuenco⁴, Susan Moore⁵
¹ Global Medical Department, Sanofi, Lyon, France, ² Lyssavirus Epidemiology and Neuropathology Unit, Institut Pasteur, Paris, France, ³ Research Institute for Tropical Medicine, Research Drive, Filinvest Corporate City, Alabang, Muntinlupa City, Metro Manila, Philippines, ⁴ Facultad de Medicina San Fernando, Universidad Nacional Mayor de San Marcos, Lima, Peru, ⁵ Veterinary Medical Diagnostic Laboratory/One Health Laboratory, College of Veterinary Medicine, University of Missouri, Columbia, Missouri, USA

In a previous systematic literature search and corresponding meta-analysis on three standard of care rabies vaccines (purified chick embryo cell vaccine [PCECV], human diploid cell culture rabies vaccine [HDCV] and purified vero cell rabies vaccine [PVRV]), a trend of higher Geometric Mean of Rabies Virus Neutralizing Antibody Titers (GMT) was observed in studies conducted before the 2000s compared to more recent studies. In this research we assessed the possible confounding factors related to these results.

We searched publications presenting Post Exposure Prophylaxis GMT at day 14 and 28 following vaccination with aforementioned vaccines from 1985 to 2022.

We conducted random-effect meta-analyses, to compute mean GMT values by vaccine type, study year, laboratory, administration route, and Rabies Immunoglobulins (RIG) coadministration.

Here we performed a meta-regression with all the eligible predictors (separated and combined).

57 articles were selected representing 90 interventional groups (n= 5,701). Year of titration was directly correlated with GMT at Day 14 and 28 (Figure 1), as well as Laboratory (Table 1). Separately, the other covariates were not found to be correlated to the GMT.

When adjusting for all the covariates (laboratory, route of administration, vaccine used, and RIG coadministration) there is still a high degree of heterogeneity, but the year of titration remains significant ($p < 0.0001$).

This observed GMT decrease trend over time persists after adjusting by other confounding factors investigated here. This trend might be explained by other circumstances such as the evolution of the assay methods and standards that may have become more stringent over time.