

## Lyssaviruses and the Evolution of Rabies: A Riddle Wrapped in an Enigma<sup>1</sup>

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### Abstract

Rabies is an important cause of human mortalities, with human cases in the developing world being mainly due to spill-overs of the rabies virus from dogs as the natural reservoir; such a source has been largely eliminated in developed countries, where bats constitute a major residual source of spill-overs. In addition, bats would appear to be the reservoir for many, if not all, other members of the genus *Lyssavirus* in the Old World, some of which may spill over into humans on occasion. Where known, the rabies and related viruses are transmitted in the saliva of an infected animal to the muscles of a potential new host by biting; thereafter, the virus spreads into and within the central nervous system and thenceforth output targets (most especially the salivary glands) for further onward transmission; this is maximised in the case of 'furious' rabies, where the virus essentially commandeers the brain towards its own ends. After reviewing current knowledge regarding the diversity of recognised species within the genus *Lyssavirus*, the nature of typical rabies infections in terrestrial mammals is reviewed, together with evidence for atypical *in vivo* investigations, in the laboratory and in the wild. Thereafter, the riddle of the nature of the effects of natural and experimental infections of rabies and other lyssaviruses in bats is reviewed. Finally, given the assumption that lyssaviruses originated from spill-over(s) of an ancestral rhabdovirus from insects into bats, consideration is given as to the enigma of how the sophisticated highly-derived cycle of the rabies virus in terrestrial mammals may have originated, and how this might also resolve the riddle presented by bats.

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<sup>1</sup> This paper will be updated based on feedback which has been sought from various authorities more intimately connected with the field: please check <http://uc.edu.kh/ucs/UC%20Publications/8/2763/> for the latest version.

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