

# EQUINE MULTINODULAR PULMONARY FIBROSIS: THE ROLE OF EHV-5 IN THE PATHOGENESIS OF AN EMERGING DISEASE

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**Introduction:** Equine multinodular pulmonary fibrosis (EMPF) is a recently described condition characterized by loss of functional pulmonary parenchyma due to extensive nodular to coalescing interstitial fibrosis. A strong association with equid herpesvirus 5 (EHV-5) has been established; however, the pathogenesis of the condition remains unclear.

**Materials and Methods:** A retrospective study of formalin-fixed, paraffin wax-embedded tissues from cases of EMPF from Europe and the USA was performed. The presence of EHV-5 DNA within lesions was demonstrated using RNA in-situ hybridization, and immunohistochemistry and electron microscopy were used to characterize the infected cells.

**Results:** Cases of EMPF were characterized histologically by multifocal to coalescing interstitial pulmonary fibrosis, with remaining alveoli lined by cuboidal epithelium (type II pneumocyte hyperplasia) and filled with inflammatory cells. EHV-5 antigen was identified within both type II pneumocytes and macrophages.

**Conclusions:** EHV-5 (a gammaherpesvirus;  $\gamma$ HV) has been isolated from both healthy horses and those with respiratory signs, at highly variable rates.  $\gamma$ HV in other species have an association with pulmonary fibrosis and repeated injury of type II pneumocytes and macrophages leads to production of transforming growth factor (TGF)- $\beta$ , which induces fibrosis (e.g. Epstein-Barr virus in human idiopathic pulmonary fibrosis). Investigation of the role of TGF- $\beta$  in EMPF is ongoing in order to further characterize the pathogenesis of EHV-5 in this emerging disease.

