# A study on the pathogenesis of canine herpesvirus encephalitis in newborn pups

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This study was done to elucidate the pathogenesis of encephalitis of newborn pups infected with canine herpesvirus (CHV).

A total of 7 newborn Beagle pups from a bitch with no history of CHV infection were experimentally infected with CHV by nasal-oral inoculation and the pups were killed one-by-one at intervals of between 1 and 2 days after the inoculation. Brains were collected at necropsy and were examined histopathologically. In addition, immunohistochemical staining and in situ hybridization (ISH) were performed to determine the distribution and localization of the CHV antigen and genome within the brain during the evolution of CHV encephalitis.

Histopathological findings of the infected brains showed the presence of nonsuppurative meningoencephalitis, characterized by microgliosis, degeneration and necrosis of neurons and glial cells, perivascular cuffing and meningeal cell proliferation. The gray matter was more severely involved than the white matter. Microscopic lesions were first seen in the brain of a pup killed at 3 days after the inoculation.

Immunohistochemically, the presence of CHV antigen in the cytoplasm of degenerative neurons and glial cells was demonstrated. Antigen positive-cells were first seen in the thalamus and hypothalamus at 4 days after the inoculation. Thereafter, CHV antigen was detected mainly in the gray matter of the ventromedial cerebrum, hippocampus, cerebellum and areas of the nucleus of the trigeminal nerve and reticularis. Vascular endothelial cells were invariably negative, but focal antigen-positive nerve and glial cells surrounding the capillaries were occasionally present. Labeling by ISH was mostly restricted to the nuclei but otherwise matched the distribution of CHV antigen.

This study demonstrated the lesions and distribution of the CHV antigen and genome in the brain of newborn Beagle pups during the evolution of CHV encephalitis for the first time. The patterns of involvement in the brain suggest olfactory and trigeminal pathways as the routes of entry in CHV encephalitis, while other findings suggestive of the infection were indicative of a hematogenous route without replication of the virus in the endothelial cells. These results can improve the understanding and characterization of the pathogenesis of CHV infection in the brain. Further investigations similar to this study will help us to understand the pathogenesis of CHV encephalitis.