The invasion routes of neurovirulent influenza virus (HK 483) into the central nervous system after intranasal inoculation in mice

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Neurovirulent avian influenza virus (HK 483) isolated at Hong kong in 1997 was inoculated intranasally to mice, and invasion routes of the virus to the central nervous system were investigated. Also, viral distribution in the mice were demonstrated using immunohistological (IH) and in situ hybridization (ISH) methods, and sensitivities of the two methods for viral detection were compared. Virus infected cells showed the viral antigens (IH method) chiefly in the nucleus, whereas the viral RNA and mRNA (ISH methods) were demonstrated in the cytoplasm around the nucleus of the cells. Viral RNA and mRNA of HK 483 might be replicated at the cytoplasm of the infected cells and the viral proteins newly synthesized from the RNAs were tranfered promptly form the cytoplasm to nucleus. IH was more sensitive than ISH for the detection of the virus in the mouse tissue.

Major histopathological changes of the intranasally inoculated mice were bronchitis, bronchointerstitial pneumonia, gangilonitis, and nonpurulent encephalomyelitis at the brain stem and anterior part of the thoracic cord. The viral antigen appeared at pterygopalatine, trigeminal and proximal ganglions prior to or simultaneously with the CNS tissues. The antigen also appeared at the olfactory bulb from the early stage of the infection. These findings suggested that intranasally inoculated HK 483 propagated at the respiratory tracts and invaded CNS (olfactory bulb, brain stem and anterior part of the thoracic cord) through the following 3 afferent nerves : olfactory, vagal and/or trigeminal, and sympathetic nerves.

Influenza virus infection of the olfactory bulb and spinal cord via olfactory and sympathetic nerves demonstrated in the present study has been reported neither in natural nor experimental infections of the virus in humans and animals. Further study is needed to clarify the contributing factors of the host and virus for substantiating the infection routes.