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rated in agnoprotein-deficient JCV, however, agnoprotein failed to directly transactivate the JCV promoter, suggesting that JCV agno-

protein up-regulates the viral propagation in some way except for viral transactivation.

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Experimental studies on encephalitis/encephalopathy due to virulent influenza virus infection

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In the present study, virulent influenza A viruses were inoculated to the chicken embryos and mice, and the primary target cells of the viruses and the mechanism for the development of encephalitis/encephalopathy were compared between them.

Virulent strains of different pathogenicity (A/tern/South Africa/61 (H 5 N 3), A/whistling swan/Shimane/499/83 (H 5 N 3 ; 24a 5 b), A/Hong Kong/483/97 (H 5 N 1), A/Hong Kong/156/97 (H 5 N 1)) or an avirulent (A/duck/Pennsylvania/10128/84 (H 5 N 2)) strain of type A influenza virus were inoculated into the allantoic cavities of chicken embryos. The virulent strains replicated initially in the vascular endothelial cells and then spread to parenchymal cells of the embryos. In contrast, the avirulent virus did not replicate in the vascular endothelial cells. Neither destruction of allantoic membrane nor disseminated intravascular coagulation were found in the embryos infected with the virulent strains. Thus, these findings suggested that the cause of death of chicken embryos was systemic viral infection after initial infection to the vascular endothelial cells.

The invasion routes of the neuropatho-

genic influenza A virus (HK483) into the CNS were investigated. The major pathological findings consisted of bronchitis, bronchopneumonia, ganglionitis, and nonpurulent encephalomyelitis in the brain stem and thoracic spinal cord. Viral antigens were demonstrated in the pterygopalatine, trigeminal and superior ganglia prior to or simultaneously with their detection in the CNS. These findings indicated that the virus reached the CNS through afferent fibers of vagal and/or trigeminal nerves. In the spinal cord, viral antigens were first demonstrated at the anterior part of the thoracic cord, sympathetic trunk ganglia, and spinal ganglia. Therefore, it was suggested that the virus initially replicated in the lungs, and ascended to the thoracic cord via cardiopulmonary splanchnic nerves, sympathetic trunk ganglia and dorsal root ganglia. The antigens were also observed in the olfactory bulb from an early stage of the infection. In this experiment, the invasion routes of the virus into the CNS via the olfactory nerves, cardiopulmonary splanchnic nerves and sympathetic nerves were newly identified in addition to the vagal and glossopharyngeal nerves.

These results suggest that the animal models may be useful to study the pathogene-

sis of human influenza encephalitis/ encephalopathy.

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Studies on the causal agent of so-called fowl glioma

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So-called fowl glioma is characterized by multiple nodular gliomatous growths associated with disseminated nonsuppurative encephalitis. The purpose of the present study was to examine the relationship between so-called fowl glioma and the causative agent. Firstly, to examine the possibility of transmissibility of the causative agents, chicks of Japanese bantams and specific pathogen-free (SPF) chickens (C/O strain White Leghorn) were intracerebrally inoculated with the brain homogenate or culture supernatant from a bantam affected with fowl glioma. All 22 bantams and 16 of 18 chickens in the inoculated groups showed nonsuppurative encephalitis, and the 18 bantams and five chickens developed multiple astrocytic nodules in the cerebrum. These astrocytes immunohistochemically had avian leukosis virus (ALV) antigen. By Southern blot analysis, the ALV proviral sequence was detected both in DNA prepared from the brains of the inoculated birds and in DNA from the inoculum. Ultrastructurally, C-type retroviruses-like particles were detected on the cell surface of the CEF inoculated with brain homogenate of chicken affected with fowl glioma. These results suggested that the gliomatous lesions of the bantams could be transmitted by in-

tracerebral inoculation of the affected tissue and the causal agent was an ALV. Secondly, the various organs as well as central nervous system were examined in SPF chickens inoculated with a brain homogenate from a bantam affected with fowl glioma. Histologically, six of eight inoculated chickens developed nonsuppurative encephalitis in the cerebrum and two of them had the characteristic lesions of fowl glioma. Hyperplastic lymphoid foci concomitantly developed in various organs of these birds, especially in the heart. Apart from these lymphoid foci, nonsuppurative myocarditis was observed in all inoculated birds. Immunohistochemically, the myocardium of all inoculated birds consistently showed strong reactivity for this antigens. These results suggest that the causal virus of fowl glioma has a high propensity to replicate especially in myocardium, and nonsuppurative myocarditis occurs associated with fowl glioma. Finally, to investigate the relationship between the proliferating astrocytes and collagen fibers in the gliomatous nodules, ultrastructural studies were performed on the initial stage of nodules from two bantams affected with naturally occurring fowl glioma. The nodule was composed of closely packed astrocytes. The proliferation of fibroblasts and