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Laboratory of Comparative Pathology

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This laboratory covers pathological diagnosis and research on various animal diseases. Field cases for the pathological diagnosis come from veterinary teaching hospital, animal hospitals, large animal clinics, zoological gardens and aquariums. Undergraduate students and post-graduate students at the first year of their Ph. D. course are obligated to undertake the diagnosis of the field cases under the supervision of the teaching staffs.

Major concern of veterinary pathology is the pathogenesis of animal diseases. Clarifying all the events occurring within the diseased animal contribute to the development of novel, more effective therapy and prevention of the diseases. Various methods including morphology, histochemistry, immunopathology and molecular pathology are available in this laboratory and many collaborative researches with other laboratories are in progress. The main research projects of the laboratory are as follows :

1. Neosporosis : Neospora is newly found an apicomplexan parasite that can cause paralysis and death in congenitally infected dogs and calves, and the disease in cattle is a significant cause of economic and reproductive loss to the livestock industry. Life-cycle of the parasite is unknown and mode of transmission except intrauterine infection to fetus remains to be elucidated. Various animal species including monkeys can be infected but a susceptibility of human to the parasite is unknown. In 1991 we reported the first cases of canine and bovine neosporosis in Japan. Since then, we found a high prevalence of the antibody in Japanese cattle herd. Our several data suggested the parasite circulates among cattle and dogs, and the parasite might be horizontally transmitted by feces. Meanwhile we have isolated and maintained 3 strains of *Neospora caninum* from bovine fetuses. Serological studies on human susceptibility, preparation for neospora vaccine, monoclonal antibody for the treatment, and ELISA kit for the rapid diagnosis are now in progress using the strains.

2. Development of animal model of Itai-Itai disease (IID) : IID of human is a complicated complaint of osteomalacia, renal anemia and tubular nephropathy caused by chronic cadmium exposure. Reproduction of IID in experimental animals has been successful only in tubular nephropathy and the lack of suitable animal model of IID prevents the establishment of the pathogenesis of IID and the reasonable criteria for the qualification of IID patients by the government, and the development of novel therapy for the patients. We have demonstrated that nephropathy, osteomalacia and renal anemia can be reproduced in ovariectomized rats by intravenous administration of cadmium for 70 weeks. This murine model was the first animal model of IID and we found a joint administration of vitamin D_3 and estrogen to the model was effective for the improvement of bone lesion. Simian model of IID is going to be established.

3. Lead poisoning in waterfowl : This toxicosis is a unique and serious disease of wild waterfowl. It results from the ingestion of spent lead shotgun pellets by birds feeding in heavily hunted areas. We have reported the first mortality associated with this toxicosis in Japan in 1992 and propose this toxicosis maybe a threat to waterfowl, but this disease still occurs in Japan. Our works suggested the pathomorphologic differences of hepatic lesions between species and we showed pathogenesis of mottled green liver in white-fronted geese was related with intrahepatic impaired excretion of bile as well as hemolysis. Experimental studies to examine the toxic effects of lead on birds are in progress. In addition, we currently investigate the prevalence of ingested

shotgun pellets among harvested waterfowl in Japan and estimate the prevalence of the poisoning in waterfowl carcasses in order to clarify the degree of environmental contamination of lead pellet.

4. Researches using molecular pathology techniques : following researches are undertaken in this laboratory ; molecular analysis of hemagglutinating ability of the rabbit hemorrhagic virus capsid protein expressed in *Escherichia coli*, expression of c-erbB-2 gene and mouse mammary tumor virus gene-like sequence in canine mammary tumors, cerebellar atrophy due to apoptosis in transgenic mice expressing human IL-2 gene.

Reference

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