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Study on effect of hyperhistaminemia on clinical features and survival times,  
and cause of hyperhistaminemia in dogs with mast cell tumor.

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Hyperhistaminemia is commonly seen and thought to be a cause of clinical symptoms in dogs with mast cell tumor (MCT). The relationship between the degree of hyperhistaminemia and clinical signs or prognosis in dogs affected with MCT has not been fully described yet. The purpose of the study reported here was to determine the significance of plasma histamine concentration as a possible prognostic marker in dogs with MCT.

The relationships between changes of the plasma histamine concentrations to the clinical signs or prognosis, histological grade and clinical stage of dogs with MCT were examined. Changes in the plasma histamine concentration showed a direct correlation with clinical signs, and can be used to predict the prognosis of dogs with MCT. Plasma histamine concentration remarkably raised to approximately 10 to 100 times higher during the critical phase than that in the early phase in the tumor. The clinical stage was related to plasma histamine concentrations in the critical phase of the dog, but not in the early phase of the dog. These results suggest that plasma histamine concentration can become an important marker in understanding the biological behavior and predicting the prognosis of dogs with MCT.

In tumor cells from dogs with MCT, histidine

decarboxylase activity (HDC), an enzymatic activity reflecting histamine synthesis, and the proliferative activity of tumor cells were examined. In cultured MCT cells from two dogs, a high proliferation rate exhibited significantly low histamine concentration both intra and extracellularly. The MCT cells with a low proliferation rate had significantly high histamine concentration. HDC activity in higher and lower proliferation were likely parallel to the intra and extracellular histamine concentrations. In nude mice with experimentally-inoculated MCT cells from three dogs, intracellular and plasma histamine concentrations had good correlations with HDC activity in tumor cells but not with tumor proliferation.

These *in vitro* and *in vivo* results suggest that HDC activity in MCT cells can be used as an indicator of histamine contained in or released from the tumor, and can be exploited as a predictive marker of hyperhistaminemia during the critical phase of patients with MCT. The measurements of HDC activity and intracellular histamine concentrations, using biopsy samples from tumors in the early phase would therefore be worthwhile in understanding the prognosis, as well as the histological grading and clinical staging of MCT.