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Author(s)	MAEDE, Yoshimitsu; TAJIMA, Motoshi; YAMATO, Osamu
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Laboratory of Internal Medicine

Professor : Yoshimitsu Maede  
Lecturer : Motoshi Tajima  
Instructor : Osamu Yamato

Teaching Staff is composed of a professor, a lecturer and an instructor. In addition, four postgraduate and six undergraduate students study on the basis of their own theme. The staff of this laboratory teach large and small animal medicine including clinical procedures to students at the fourth and fifth grades. Also the staff teach clinical medicine, clinical medicine training, to students at the Veterinary Teaching Hospital.

In research field, this laboratory has been studying on the pathogenesis of erythrocyte disorders, especially hemolytic anemia. In a different line of research, this laboratory is also investigating the molecular mechanisms of several genetic disorders in domestic animals.

Prof. Maede has reported 2 canine cases of acute hemolytic anemia after eating a small quantity of onion in 1977. In the course of the study to clarify the mechanism of anemia induced by onion, he has found that some dogs have erythrocytes characterized by high Na, K-ATPase activity with high K and low Na concentration (HK RBCs), whereas normal canine erythrocytes completely lack the enzyme and have high Na and low K concentrations (LK RBCs). He has demonstrated that the Na gradient-dependent L-glutamate and L-aspartate transport in the HK RBCs are markedly increased by the large gradient of Na and K across the cell membrane induced by the Na, K-ATPase, resulting in the high accumulations of the amino acids and reduced glutathione (GSH) in the cells. He has examined Na and K concentrations and Na, K-ATPase activity in erythrocytes from 24 Japanese Shiba dogs and 79 dogs of 24 other breeds, and found that eleven of the Shiba had

HK RBCs, while the cells from the remaining dogs had LK RBCs. From the results, he considers that the gene for HK RBCs may be inherent in dogs indigenous to Japan, particularly in Shiba dogs.

The our research activities are as follows.

1. Studies on canine erythrocytes with hereditary high Na, K-ATPase activity and high concentrations of potassium, reduced glutathione (GSH) and some amino acids.

1) Maede, Y., Inaba, M. and Taniguchi, N. 1983. Increase of Na, K-ATPase activity, glutamate and aspartate uptake in dog erythrocytes associated with hereditary high accumulation of GSH, glutamate, and aspartate. *Blood*, 61 : 493-499.

2) Inaba, M. and Maede, Y. 1984. Increase of Na gradient-dependent L-glutamate and L-aspartate transport in high activity of (Na, K) -ATPase. *J. Biol. Chem.*, 259 : 312-317.

3) Maede, Y., Kuwabara, M., Sasaki, A., Inaba, M. and Hiraoka, W. 1989. Elevated glutathione accelerates oxidative damage to erythrocytes produced by aromatic disulfide. *Blood*, 73 : 312-317.

2. Studies on the pathogenesis of anemia in dogs infected with *Babesia gibsoni*.

1) Murase, T. and Maede, Y. 1990. Increased erythrophagocytic activity of macrophages in dogs with *Babesia gibsoni* infection. *Jpn. J. Vet. Sci.*, 52 : 321-327.

2) Murase, T., Iwai, M. and Maede, Y. 1993. Direct evidence for preferential multiplication of *Babesia gibsoni* in young erythrocytes. *Parasitol. Res.*, 79 : 269-271.

3) Murase, T., Ueda, T., Yamato, O., Tajima, M. and Maede, Y. 1996. Oxidative damage and enhanced erythrophagocytosis in canine erythrocytes infected with *Babesia gibsoni*. *J. Vet. Med. Sci.*, 58 : 259-261.

3. Studies on the mechanism of onion-induced hemolytic anemia in domestic animals.

- 1) Yamato, O. and Maede, Y. 1992. Susceptibility to onion-induced hemolysis in dogs with hereditary high erythrocyte reduced glutathione and potassium concentrations. *Am. J. Vet. Res.*, 53: 134–137.
- 2) Yamato, O., Yoshihara, T., Ichihara, A. and Maede, Y. 1994. Novel Heinz body hemolysis factors in onion (*Allium cepa*). *Biosci. Biotech. Biochem.*, 58: 221–222.
- 3) Yamato, O., Hayashi, M., Yamasaki, M. and Maede, Y. Sodium *n*-propylthiosulfate is one of the causative agents of onion-induced haemolytic anaemia in dogs. *Vet. Rec.*, (in press).
4. Studies on the pathogenesis of bovine viral diarrhoea mucosal disease
  - 1) Tajima, M., Yazawa, T., Hagiwara, K., Kurosawa, T. and Takahashi, K. 1992. Diabetes mellitus in cattle infected with bovine viral diarrhoea mucosal disease virus. *J. Vet. Med. series A*, 39: 616–620.
  - 2) Tajima, M., Kirisawa, R., Taguchi, M., Iwai, H., Kawakami, Y., Hagiwara, K., Ohtsuka, H., Sentsui, H. and Takahashi, K. 1995. Attempt to discriminate between bovine viral diarrhoea mucosal disease virus strains using polymerase chain reaction. *J. Vet. Med. series B*, 42: 257–265.
- 3) Taniyama, H., Ushiki, T., Tajima, M., Kurosawa, T., Kitamura, N., Takahashi, K., Matsukawa, K. and Itakura C. 1995. Spontaneous diabetes mellitus associated with persistent bovine viral diarrhoea (BVD) virus infection in young cattle. *Vet. Pathol.*, 32: 221–229.
5. Studies on the diseases in wildlife caused by the pollution of the environment
  - 1) Murase, T., Horiba, N., Goto, I., Yamato, O., Ikeda, T., Sato, K., Jin K., Inaba, M. and Maede, Y. 1993. Erythrocyte ALA-d activity in experimentally lead-poisoned ducks and its change in the course of treatment with disodium calcium EDTA. *Res. Vet. Sci.*, 55: 252–257.
  - 2) Murase, T., Ikeda, T., Goto, I., Yamato, O., Jin, K. and Maede, Y. 1992. Treatment of lead poisoning in wild geese. *J. Am. Vet. Med. Assoc.*, 200: 1726–1726.
  - 3) Yamato, O., Goto, I. and Maede, Y. 1996. Hemolytic anemia in wild seaducks caused by marine oil pollution. *J. Wildlife Diseases*, 32: 381–384.