

In: **Genes, Dogs, and Cancer: Emerging Concepts in Molecular Diagnosis and Therapy**, J. F. Modiano (Ed.)
Publisher: International Veterinary Information Service (www.ivis.org), Ithaca, New York, USA.

Free Radical and Antioxidant Properties of Blood and Lymph Nodes of Healthy Dogs and Dogs with Lymphoma (21-May-2001)

P. Vajdovich¹, T. Kriska², M. Mézes³ and P. Ribiczey Szabó⁴

¹Department of Internal Medicine and Clinics, Faculty of Veterinary Science, Szent István University, Budapest, Hungary;
²Department of Oxidation Processes, Institute of Chemistry, Chemical Research Center, Hungarian Academy of Sciences, Budapest, Hungary; ³Department of Nutrition, Faculty of Agriculture and Environmental Sciences, Szent István University, Gödöllő, Hungary; ⁴Department of Internal Medicine and Clinics, Faculty of Veterinary Science, Szent István University, Budapest, Hungary.

Recent studies report that oxidative stress caused by oxygen free radicals can inhibit the ability of some chemotherapy drugs to induce apoptosis. The hypothesis for this study was that decreased sensitivity to free radical damage plays a role in maintaining cell proliferation of tumor cells, while they have a decreased antioxidant defense. For this study, we examined the difference between antioxidant parameters in blood and lymph nodes of healthy dogs and dogs with lymphoma. Subjects consisted of healthy beagle dogs, and dogs with stage III, IVa, and IVb generalized multicentric lymphoma. The healthy dogs were beagles (four males, six females) between 1.5 and 2 years old, housed in kennels. The dogs with lymphoma included two Rottweilers, two German shepherds, two bull mastiffs, one Staffordshire terrier, one Hungarian vizla, one Hungarian kuvasz, one German vizla, and 1 mix breed dog housed indoors and outdoors at the owners' residence. Seven dogs were males, four were females, their ages ranged between 3 and 8 years. The clinical stage of the disease was stage III for three dogs, stage IVa for seven dogs, and stage IVb for one dog. Histological and immunohistochemical analyses of lymph nodes from normal dogs showed no abnormalities in 2 samples, mild follicular hyperplasia in 4 samples, chronic inflammatory processes in 5 samples, and mild eosinophilic and granulocytic infiltration in four samples. There were no abnormalities in the distribution of CD3⁺ cells (T lymphocytes) and CD79a⁺ cells (B lymphocytes); occasional proliferating cells (Ki67⁺) were identified. Histological and immunohistochemical analyses of lymph nodes from dogs with lymphoma, based on the REAL classification, showed that seven cases had follicular center cell lymphoma (B cell type), three cases had B cell lymphoblastic lymphoma, and one case had Burkitt-like lymphoma. Focal areas of CD3⁺ cells were present in all malignant lymph nodes. The proliferative cell fraction (Ki67⁺) was 50 - 55% in five dogs, 55 - 60% on two dogs, 60 - 70% in three dogs, and 80 - 90% in one dog. Free radical and antioxidant parameters measured in blood and lymph nodes included reduced glutathione-concentration (GSH), oxidized glutathione concentration (GSSG), reduced and oxidized glutathione ratio (GSH/GSSG) glutathione-peroxidase activity (GSH-Px), concentration of thiobarbituric-acid reactive substances expressed in malondialdehyde (MDA), superoxid-dismutase activity (SOD), total antioxidant status, based on the reduction of iron, concentration of vitamins C and E, total free radical concentration analysed by electron spin-resonance-spectroscopy (ESR), and phorbol myristate acetate (PMA) induced free radical production analysed by chemiluminescence spectroscopy. The results show that SOD activity was 92% higher and GSH concentration was 24% lower in RBC-hemolysate of dogs with lymphoma than in RBC-hemolysate of healthy dogs, with no significant alterations in other parameters. There was a 79% decrease in SOD activity, 34% decrease in GSH-concentration and a 65% decrease in GSH/GSSG ratio in lymph node homogenates from dogs with lymphoma compared to lymph node homogenates from healthy dogs. The total free radical concentration was increased by 56%, and the PMA-induced free radical production was reduced by 97% in the lymph node homogenates from affected dogs as compared to that of healthy dogs. These results suggest that protection against free radicals by antioxidant defense mechanism is weaker in dogs with lymphoma than in healthy dogs. The observation that there are greater levels of steady-state free radicals in tumor cells may be due to an increased metabolic rate, while that PMA could not induce free radical formation in the cells from malignant lymph nodes may be due to a distinct mechanism, probably due to an altered NADPH-oxydase function.