New Study Reports Golden Retrievers Among Breeds with Low IgA Levels

Swedish researchers count Golden Retrievers among eight breeds in which 10 percent or more of adult dogs have low blood immunoglobulin A (IgA) levels. Low levels of IgA are often accompanied by recurrent infections and autoimmune and allergic diseases just as in humans with IgA deficiency.

The study was the first to evaluate IgA in several breeds of dog. Earlier research attributed low IgA levels to conditions such as atopic dermatitis and inflammatory bowel disease in German Shepherd Dogs (Tengvall, et al., 2013) and Chinese Shar-Pei. The current study found that 45 percent of Chinese Shar-Pei and 14 percent of German Shepherd Dogs were low in IgA levels.

“We found IgA concentrations to vary widely among breeds,” says researcher Katarina Tengvall, MSc, a doctorate student in genetics at Uppsala University in Sweden. “This pronounced difference may explain why there is no established normal range of IgA and accepted cutoff value for low IgA in dogs.”

“These findings are important because low IgA may be associated with an elevated risk of atopic dermatitis (atopy) and inflammatory bowel disease (IBD),” says Rhonda Hovan, research facilitator for the Golden Retriever Club of America (GRCA) and member of the club’s Health & Genetics Committee.

“Atopy and IBD are autoimmune diseases, and Goldens appear to have an elevated risk for a number of autoimmune diseases. The category of autoimmune diseases also includes hypothyroidism (autoimmune thyroiditis), masticatory muscle myositis, autoimmune hemolytic anemia, lupus (systemic lupus erythematosus), Addison’s disease (hypoadrenocorticism), rheumatoid arthritis, and myasthenia gravis.”

A part of the secretory immune system, IgA is an antibody produced by plasma cells, which protect the lining of mucosal

Canine Mammary Cancer Study Modeled After Advances in Human Stem-Cell Research

Mammary cancer is as familiar to dog breeders and owners as breast cancer is to people whose loved ones have been diagnosed with the devastating disease. Research of human mammary stem cells provides a model for research in dogs that may help advance the use of drugs to inhibit the growth potential of cancer cells.

A study underway at the Baker Institute for Animal Health at Cornell University is evaluating the role of citrullination, a cellular process mediated by peptidyl-larginine deminase (PAD) enzymes, in canine mammary cancer. PAD activity, which is usually low in healthy tissues, often increases during mammary cancer development, says lead investigator Gerlinde Van de Walle, DVM, PhD, assistant professor.

The collaborative study includes Scott
sites from pathogens. In people, IgA deficiency is associated with frequent respiratory illness and urinary tract and intestinal infections. In both dogs and people, there is no treatment for low blood IgA; rather, signs of disease are treated to help alleviate illness.

In the May 2014 issue of Veterinary Immunology and Immunopathology, the researchers indicated that low IgA in purebred dogs is likely due to founder effects, breeding practices and reproductive isolation.

“In an earlier study, we reported low IgA concentrations in wolves, the wild ancestor of the domestic dog,” Tengvall says. “Although that study used the Scandinavian wolf population, which is known to be highly inbred with very low genetic variation, this suggests that risk alleles predisposing to low IgA may have been transferred from wolves to dogs during domestication.”

A Model for IgA Deficiency

The Swedish study included 1,267 dogs representing 22 breeds. Blood samples were collected from healthy dogs and those affected by diseases living in the U.S., Sweden and Switzerland in cooperation with their owners and veterinarians. Disease-affected dogs suffered from conditions such as atopic dermatitis, Shar-Pei auto-inflammatory disease, Addison’s disease, pancreatic acinar atrophy, diabetes mellitus, and steroid-responsive meningitis arteritis.

Besides 168 Golden Retrievers, the study included 141 Labrador Retrievers and 11 Nova Scotia Duck Tolling Retrievers. The findings showed that 13 percent of Golden Retrievers have low IgA, 12 percent of Labrador Retrievers and 20 percent of Nova Scotia Duck Tolling Retrievers.

The researchers evaluated the sex of the dogs and whether spaying or neutering contributed to low IgA. In both cases, they found no correlation.

Golden Retrievers were among six new breeds recognized as having an increased risk of low IgA. The other breeds were Hovawart, Norwegian Elkhound, Nova Scotia Duck Tolling Retriever, Bull Terrier, and Labrador Retriever.

Nearly half the Golden Retrievers in the study had signs of canine atopic dermatitis, yet their IgA levels were not much lower than those of unaffected dogs. Despite this finding, it is possible that low IgA levels could be a contributing factor to immune problems in the breed.

“Although a great deal of research has been done to identify the causes of human autoimmune diseases, much less research has been done in dogs,” Hovan says. “Still, the same overall principles of autoimmune disease apply to dogs.”

An online survey conducted by the Orthopedic Foundation for Animals for the Golden Retriever Club of America indicates that 13.4 percent of Golden Retrievers have skin disease, such as atopic dermatitis, says Ann Hubbs, DVM, PhD, chair of the GRCA health and genetics committee. She says about 5 percent of the owners of Golden Retrievers also reported gastrointestinal diseases.

Alan Mundell, DVM, DACBD, a board-certified veterinary dermatologist who practices in Edmonds, Washington, says, “Due to the frequency of skin problems in Goldens, we test for IgA levels as part of our diagnostic workup, especially if a dog shows signs of allergies and infections at a young age. In my experience, Golden Retrievers are among the top four breeds for low IgA levels. Environmental influences are important as well.”

Tengvall agrees. “Genetic and environmental factors contribute to diseases affected by low IgA. The connection between low IgA levels and atopic dermatitis seems to be unique in different breeds because in Golden Retrievers there was no correlation but in German Shepherd Dogs there was.”

“The genetic components of autoimmune diseases are very complex,” Hovan says. “Genes play a role in increasing susceptibility to autoimmune diseases, but environmental triggers initiate the onset of clinical signs. In dogs that are predisposed to autoimmune reactions, there are suspected triggers, but most of the time, it is impossible to know with certainty what triggers the onset of an autoimmune disease.”

The low IgA breeds identified in the study will potentially provide genetic models to help advance understanding of IgA deficiency in people. “Dogs offer an advantageous comparative model for human disease,” Tengvall says. “We have identified six new potential genetic models of IgA deficiency.”

Thanks to this study, owners and breeders of Golden Retrievers that develop recurrent infections and autoimmune and allergic diseases can now recognize that IgA could be a contributing factor. Insights from the study also will help veterinarians who treat dogs to consider whether low IgA levels may contribute to the dog’s illness. However, as noted by the researchers, additional studies are needed to better understand the implications of low IgA levels in each specific breed, including the Golden Retriever.
Coonrod, PhD, the Judy Wilpon associate professor of cancer biology at Cornell University Laboratory of Epigenetics and Cancer Biology. His research in human breast cancer cell lines provides the basis for the canine study.

“We are basically studying whether the cancer stem-cell lines in dogs, as in people, express higher levels of PAD enzymes and whether drugs that inhibit the function of these enzymes can reduce the tumorigenicity of these cancer cells,” Van de Walle says. “If this is indeed the case, it is possible in the future that we could evaluate in clinical trials whether PAD inhibitor drugs can provide a novel treatment option for mammary cancer in dogs.”

Common in Intact Females
Mammary cancer is the most common type of tumor in intact female dogs. Studies showing that females almost never get this form of cancer if they are spayed before their first estrous cycle, which occurs around 6 months of age, indicate that the disease is closely associated with the production of reproductive hormones, principally estrogen. These studies found that the risk of mammary cancer is reduced to 0.5 percent if spaying occurs before 6 months of age, to 8 percent if spayed after the first cycle, and to 26 percent if spayed after the second cycle.

Neutering greatly reduces the risk of mammary cancer, but this isn’t a possibility for breeders and exhibitors who show dogs in conformation or compete with them in field trials. Breeders often plan to include these females with quality traits in their breeding programs to perpetuate their bloodlines.

According to the American College of Veterinary Surgeons, one-quarter of unspayed female dogs will develop a mammary tumor during their lifetime. Although rare, mammary cancer also can occur in male dogs. Spaying before the first estrous cycle (around 6 months of age) reduces the risk of mammary cancer to 0.5 percent. Early recognition of signs of mammary cancer offers hope that treatment may provide a cure.

Did You Know?
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Some do get a second form of mammary cancer. The research is funded by the Morris Animal Foundation with support from the American German Shepherd Dog Charitable Foundation and the Bichon Frise Club of America.

“The mammary stem cells are a small population of cells present in the mammary gland, yet they are the driving force behind regeneration of the gland,” explains Van de Walle. “These cells remain in the tissue for a long time, thus there is a greater chance of them becoming tumors when compared to normal adult cells that die and are replaced by new cells.”

In his work in human breast cancer, Coonrod showed that the binding of estrogen to the estrogen receptor appears to attract PAD2 enzymes to genes that promote the complete removal of malignant mammary tumors.
Remote tumor growth. As a result, the PAD2 enzymes citrullinate genes that increase transcriptional activity and promote expression of proteins involved in tumor progression.

Citrullination is a process in which positively charged arginine residues are changed to neutral citrulline residues, thus changing the charge of proteins. “This process changes a protein’s three-dimensional structure and affects how it interacts with other proteins on other cells,” Van de Walle says. “PAD2 enzymes catalyze the conversion of protein-bound arginine to citrulline.”

PAD inhibitors are drugs that inhibit PAD enzymes and thus may have an anti-tumor effect. “Our preliminary studies indicate that PAD inhibitors reduce the tumorigenic potential of canine mammary cancer cells, and they also do not harm healthy mammary cells. We are working on determining the relation between PAD inhibitors and PAD expression and function in dogs with mammary cancer.”

The goal is to study the efficacy of PAD inhibitors in a clinical trial of dogs with mammary cancer. “Before we can evaluate these drugs in dogs with mammary tumors, we need to be sure the drugs are safe at a therapeutic dose,” says Van de Walle.

The future holds promise that PAD inhibitors may one day provide an effective treatment for canine mammary cancer. In the meantime, owners should be diligent about checking their dogs for signs of cancer before it spreads. The earlier a mass is found and surgery is performed to remove it, the better chance there is for a successful outcome.

‘Matisse’ Wins Pro Plan Champions Cup

After leading the pack all year, GCH Claircreek Impression De Matisse has won the 2014 Pro Plan Champions Cup by earning 480 points through Dec. 31. The 3 1/2-year-old male Portuguese Water Dog, called “Matisse,” was bred by Donna Gottdenker, who co-owns him with Milan Lint and Peggy Helming. Professional handler Michael Scott handles Matisse, who finished second in the 2013 Champions Cup competition.

The yearlong Pro Plan Champions Cup award, which is sponsored by Purina Pro Plan brand dog food, is based on points tabulated from Bests in Show and Group placements at more than 200 Purina-sponsored all-breed dog shows. The winner receives a $10,000 cash prize, an original oil painting by dog portrait artist Linda Draper and a keepsake Pro Plan Champions Cup trophy.

Take a look and see if you recognize the Top 10 placing dogs.

Upcoming Events

Check out upcoming Purina-sponsored show and sporting events at venues across the country. These events are opportunities to meet dog enthusiasts, canine experts and Purina representatives.

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