

## Investigation of Gallbladder Disease and Hypercholesterolemia in Shetland Sheepdogs\*

March 2008, Updated December, 2008, May 2009, November 2009, August 2010

### NEWS FLASH!!! Genetic Mutation Found and Research Results Published!

Dr. Katrina Mealey, primary investigator of the study, reported to the ASSA Research Advisory Committee in September, 2009 that her group had identified a genetic mutation in Shelties that was strongly associated with gallbladder mucoceles. Dr. Mealey's group is the same one that developed the DNA test for the MDR-1 gene. **The research results were published in *Comparative Hepatology* in July, 2010.**

Mealey KL, Minch JD, White SN, Snekvik KR, Mattoon JS: An insertion mutation in ABCB4 is associated with gallbladder mucocele formation in dogs. Comp Hepatol. 2010 Jul 3;9:6.

A genetic mutation that likely plays a role in the formation of gallbladder mucoceles in dogs was found. Median age of affected Shelties was 9 yrs (range 5-12 yrs). Although not yet proven, the authors believed that the occurrence of gallbladder mucoceles in dogs is inherited as a dominant trait with incomplete penetrance. None of the affected dogs was homozygous for the mutation. Because people who are homozygous for a similar mutation have very severe disease, the authors speculated that dogs homozygous for the mutation might die, either during embryonic development or in early puppy-hood.

The discovery of the mutation may be used, in the future, to identify dogs predisposed to gallbladder mucocele formation at an early age. This would allow these dogs to be closely monitored for mucocele formation. Surgical intervention could be performed before disease-induced morbidity places the patient at higher risk for intra- and post-operative complications. Also, early medical or dietary management might be used to prevent or delay the onset of gallbladder mucocele formation.

The article is available to the public through PubMed (using the website below, click on the tab in the right corner, "Free in PMC"): <http://www.ncbi.nlm.nih.gov/pubmed/20598156>

As of August, 2010, Dr. Mealey's group is studying approximately 100 samples (Shelties and other breeds) from North Carolina State University (through their pathology laboratory) which should give them more information. If they do not find a dog that is homozygous for the mutation in those samples, they will ask for the ASSA's help in contacting breeders in an attempt to identify heterozygous breeding pairs so to determine what happens to puppies that are homozygous for the mutation.

At the present time, Dr. Mealey does not need DNA samples from affected dogs unless they very young for having a mucocele (less than 5 yrs of age). If anyone has a Sheltie that fits that criterion, Dr. Mealey would like to obtain DNA via cheek swabs from such a dog. Dr. Mealey can be contacted via e-mail at: [kmealey@vetmed.wsu.edu](mailto:kmealey@vetmed.wsu.edu).

## Earlier Information and Study Background

Dr. Mealey said, "We sincerely appreciate the cooperation we have received from the American Shetland Sheepdog Association and we will keep you apprised of developments." Sheltie owners and the ASSA played an important role in providing Dr. Mealey with the material needed to identify the mutation. It was only 18 months from the time the ASSA became involved in distributing information about the study in March of 2008 until the discovery of the mutation was announced in September, 2009! **A special thank you to everyone who participated!**

Study Background: Gallbladder disease has been recognized with increasing frequency in dogs since the late 1990's<sup>1-3</sup>. Whether or not this was the result of a true increase in disease prevalence or simply the result of increased detection is unclear. Some have suggested that incorporation of abdominal ultrasound examination in dogs as a routine diagnostic tool has resulted in increased detection of gallbladder disease<sup>2</sup>. Several articles describing gallbladder mucoceles (severe distention of the gallbladder caused by a thick mass of sludge and mucus) in dogs suggest a breed predilection for the problem in Shetland Sheepdogs as well as Cocker Spaniels and Miniature Schnauzers. Both Shetland Sheepdogs and Miniature Schnauzers are breeds predisposed to hyperlipidemia (too much lipid or fat in the blood),<sup>4,5</sup> a factor that is known to contribute to gallbladder disease in people<sup>6,7</sup>. A study has confirmed a link between hyperlipidemia and hypercholesterolemia (high blood cholesterol levels) and gallbladder mucocele formation in Shetland Sheepdogs<sup>2</sup>. Collectively, this suggested the possibility of a genetic defect in a protein responsible for lipid homeostasis (regulation of blood lipid levels). In March, 2008, The Veterinary Clinical Pharmacology Laboratory, led by Dr. Katrina Mealey, at Washington State University began a research study investigating a gene that plays an important role in lipid homeostasis. It was proposed that a defect in that gene could be the underlying cause of gallbladder disease in Shetland Sheepdogs.

The ASSA assisted Dr. Mealey in collection of DNA samples from Shelties with and without hyperlipidemia and gallbladder disease by sending notice of the study through Sheltie related internet message groups and posting the information on the ASSA web page. Nine months after the study began, enough material was obtained, through the generous participation of Sheltie owners, to limit sample collection to dogs with surgically confirmed gallbladder mucoceles and older normal Shelties. As noted above, it was a mere 18 months from the beginning of ASSA participation until the genetic mutation was confirmed. This could not have been accomplished without the enthusiastic participation of Sheltie owners, and of course, without the dedication and expertise of Dr. Mealey

Dr. Mealey said, "*I was surprised (in a positive way) on the response!... Thanks for your assistance--for an uncommon disease we were able to collect a good number of samples with complete medical information in a short time period (especially considering this was breed specific!)*". **Thanks to everyone who has participated.**

**THANK YOU Dr. Mealey!!!**

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<http://www.vetmed.wsu.edu/depts-VCPL/instructions.aspx>

Additional information about gallbladder mucoceles including photos of one can be found at the following link on DVM 360:  
<http://veterinarymedicine.dvm360.com/vetmed/article/articleDetail.jsp?id=591378&sk=&date=&pageID=2>.

### **References**

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\* This report will be updated as new information is received and when the DNA test becomes commercially available.