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BHCA Health Committee

Emerging Health Issues Bulletin

TOPIC TITLE: Mucopolysaccharidosis (MPS1) Testing at the Denver Nationals

Starting with this first edition, the BHCA Health and Research Committee will publish Emerging Health Issues Bulletins as we delve into health concerns that affect Basset Hounds. We recently became aware of an emerging genetic disease in Basset Hounds for which a test has just been developed and validated, and have arranged for cost-free, non-invasive testing at the Denver Nationals. We are issuing this first bulletin to ensure that BHCA members attending the Nationals are aware of this opportunity. In addition, we want members to know of a discounted cost for primary open angle glaucoma (POAG) tests from the Animal Health Trust in Great Britain. Please see below for details.

The Committee is working to determine which issues to focus on in future Bulletins and which researchers to work with, but for now, getting the information out on testing for MPS1 and POAG at the Nationals is our top priority.

Background:

In the past few months, mucopolysaccharidosis (MPS1) has been clinically and genetically confirmed in Basset Hounds from multiple BHCA-member kennels. MPS1 is one of several *lysosomal storage diseases*, a group of inherited metabolic disorders that result from defects in the function of lysosomes. Lysosomes are the "recycling center" in cells that, when functioning normally, process unwanted or worn out material in a cell into components that the cell can use. The lysosomes use enzymes to do this processing, and if one or more of these enzymes is absent or exists only in small amounts, the recycling process doesn't work. Unprocessed material then accumulates in the cell. Eventually the stored material builds up so much that the cell can no longer function. When this happens in enough cells, disease symptoms appear.

MPS1 usually manifests in puppies around 6-8 weeks of age. Most affected puppies do not survive. The disease can take several forms, including cranial abnormalities, skeletal deformities, cloudy eyes, webbed feet, dwarfism, and loss of the ability to walk. Puppies may display one or more of these symptoms, which can vary in severity. Affected dogs that survive puppyhood rarely live to the age of 2 years. Several types of MPS exist and can affect dogs, cats, and humans. To date, MPS1 has been documented in Plott Hounds, Rottweilers, and Boston Terriers. Because it has been, until now, unknown in Basset Hounds, it is likely that prior cases have been misdiagnosed as "fading puppy syndrome", birth defects, or some other cause such as encephalitis or hydrocephaly.

MPS1 is caused by the inheritance of two copies of a recessive gene that has the mutation for MPS1. When two normal-appearing dogs that carry the mutation are bred and a puppy (or puppies) gets the recessive gene from **BOTH** parents, that puppy (or puppies) is affected by MPS1. Pups in the litter that do **not** inherit the recessive gene from both parents will not become ill, though some may be carriers (with one normal dominant gene and a recessive one carrying the mutation).

Example: Dominant "M" or recessive "m" are the forms of the gene contributed by each parent. Each offspring will have a combination of the two (MM, Mm, mm).

Homozygous normal/clear (MM) bred to Homozygous normal/clear (MM)

	M	M	
M	MM	MM	All offspring can only be homozygous clear
M	MM	MM	

Homozygous normal/clear (MM) bred to Heterozygous carrier (Mm)

	M	M	
M	MM	MM	50% of offspring are homozygous clear
m	Mm	Mm	50% of offspring are heterozygous carriers

Heterozygous carrier (Mm) bred to Heterozygous carrier (Mm)

	M	m	
M	MM	Mm	25% of offspring are homozygous clear 50% of offspring are heterozygous carriers 25% of offspring are homozygous affected
m	Mm	mm	

Homozygous affected (mm) bred to homozygous affected (mm)

	m	m	
m	mm	mm	All offspring can only be homozygous affected
m	mm	mm	

Although the disease is devastating, there is good news. The University of Missouri (MU) has developed and validated a genetic test for the variant found in the Basset Hound, and dogs can be tested to identify those who carry the mutation or are clear of it. Breeding a dog with one copy of the mutation (heterozygous carrier) to one who tests clear (homozygous normal) will produce **no** affected dogs and, with testing to know which of the puppies are carriers, it is possible to breed away from the mutation and, over a few generations, clear it from the line of dogs in which it appeared. Doing this is important not only for preserving health in that line of dogs, but also for continuing to safely breed dogs from the line and preserve their positive contributions to genetic diversity within the breed.

Significance:

The MU College of Veterinary Medicine identified the genetic mutation for MPS1 in three related Basset Hounds diagnosed with MPS1 (homozygous affected) and confirmed, through genetic testing, that several of those dogs' relatives were carriers. The next step is to estimate how widely the mutation is disseminated within the breed. In conjunction with the BHCA Health and Research Committee, and with a grant from the BHCA Foundation, MU will be providing cost-

free tests at the Denver Nationals to assess how widespread the MPS1 mutation is within the breed. Individual test results will be provided to owners – and to no one else – in 1-2 months. If other carriers are found, the test will be made more broadly available.

Alongside the previously publicized swab clinic for primary open angle glaucoma (POAG), the BHCA Health and Research Committee will be collecting swabs for MPS1 at the Denver Nationals on Monday, September 30, 2:00-3:30pm. The costs of the MPS1 are being underwritten by the BHCA Foundation and you can have up to 3 dogs tested at no cost to you. The fee for POAG testing is approximately $40.

Actions: To sign up for the tests and what you will need

If you wish to get dogs tested at the Nationals for either MPS1 and/or POAG, please send your name and the number of dogs you want tested for each to Sylvie McGee (sylviemcgee@gmail.com) by September 20th. This will help us ensure that we have enough test kits to accommodate everyone who wants to get dogs tested. If you are unable to attend the swab clinic on September 30th you can arrange an appointment for another time/day at Nationals by contacting Sylvie.

The test for **MPS1** is free of cost to persons attending the Nationals and available for up to 3 dogs per person. For each dog tested, you need to bring the dog and a written copy of its 4-5 generation pedigree to submit with the test. MU will contact you directly with test results. For persons not attending the Nationals, stay tuned. The MPS1 test is not yet available elsewhere, but we will let members know when it is.

For the previously announced testing for **Primary Open Angle Glaucoma,** the cost (after a 20% discount for BHCA members) is approximately $40.00, payable by credit/debit card at the time of testing. Your card will be charged directly by the Animal Health Trust (AHT) in England. For this test you need your dog, the dog's AKC registration number, microchip # (if applicable), and a credit/debit card number for billing. All documentation on dogs and billing information will remain confidential and in individually sealed security envelopes through the shipping process. The AHT will contact you – and you only - directly with test results.

For persons not attending this year's Nationals, you can still obtain the discount by going to the AHT website (https://www.ahtdnatesting.co.uk/) before December 31st, 2019, ordering a test kit to be mailed to you, and entering the code "POAG2019" in the space labeled "discount" on the billing page.

IMPORTANT NOTE: For both tests, in order for test results to be valid, food and water must be withheld for 2 hours prior to testing.

Health & Research Committee Contact:

For more information, contact Rosemary Ryan, Chair, BHCA Health and Research Committee, R2ryan46@wavecable.com, 206.687.0891.

References:

- http://www.akcchf.org/research/research-portfolio/2604.html
- https://wagwalking.com/condition/mucopolysaccharidoses