Mary Mahaffey's DMS Quiz
Thank you so much Mary!

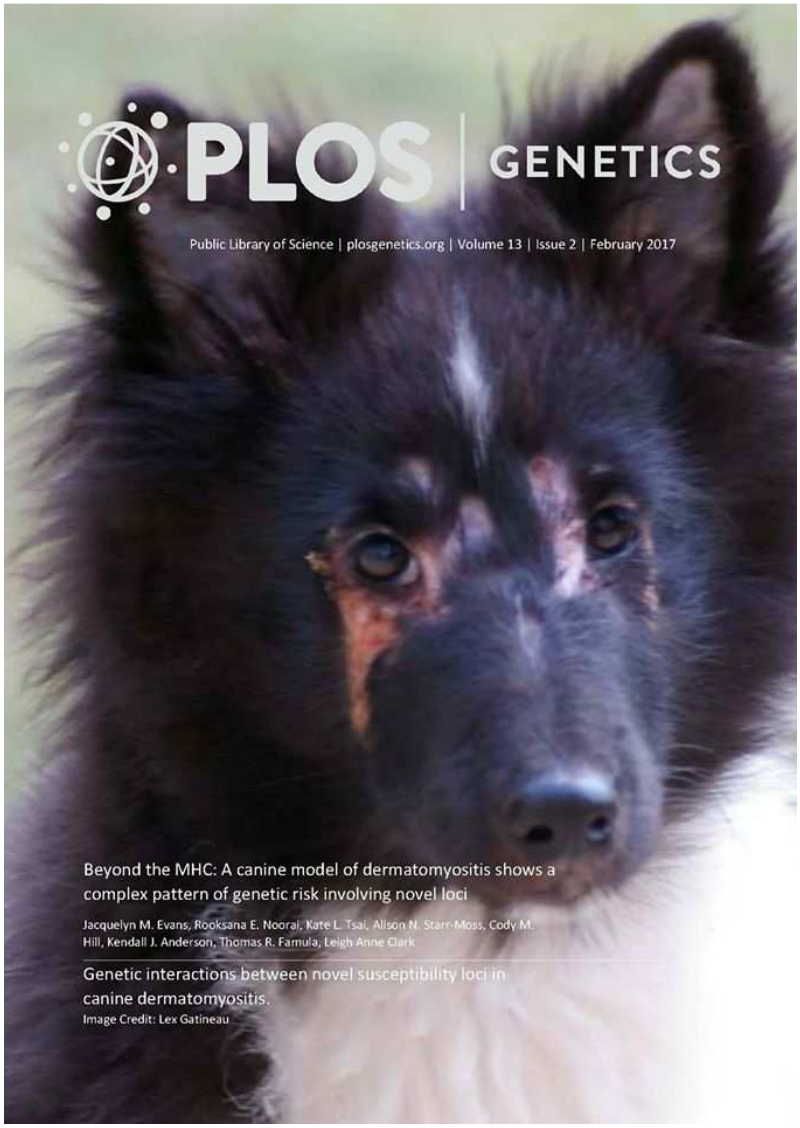
DMS practice quiz #1. The answer is in the comment section below.

Because there have been some questions and discussion about the new DNA test for dermatomyositis, I thought I would try to stimulate more discussion by posting some daily "quizzes" on the topic. Here's the first one.

You have a bitch with the following genotype, DLA 002:01/002:01 aabb. You don't have to worry about knowing the genotype of any stud you might consider for her because all of her pups will have low risk genotype no matter the genotype of the stud. TRUE or FALSE?

Go to the following webpage, http://americanshetlandsheepdogassociation.org/dermatomyos…/ , to find the answer either by using the "Genotype Calculator" or by clicking on the Punnett square link. I'll provide the answer tomorrow.

Answer: True! You could breed her to a stud with the AABB genotype (so far 100% of dogs with this genotype have been affected) and all pups would be AaBb which is low risk!



DMS practice quiz # 2: The answers to this quiz are in the comment section below.

You have a beautiful bitch with the following genotype, 002:01/023:01 AaBb. Which of the following statement(s) is/are true? (Answers will be provided tomorrow, but you can find answers earlier by going to: http://americanshetlandsheepdogassociation.org/dermatomyos…/ .)

a. DLA 002:01, A, and B are risk alleles for DMS....
b. Since this is a moderate risk genotype, you should not breed her!
c. This is a low risk genotype and you can breed her to any stud with low risk genotype and not be concerned about producing pups with dermatomyositis.
d. She has the DLA 023:01 allele which is highly desirable!

Answer to DMS practice quiz # 2: – A and D are TRUE.
a. TRUE. DLA-DRB1*002:01 is a risk allele. See "d" below. The normal (aka "wild type") alleles of loci A and B are represented by lower case letters, a and b, while the risk alleles are A and B.

b. The 002:01/023:01 AaBb genotype is low risk, not moderate. See http://americanshetlandsheepdogassociation.org/dermatomy.../ for a listing of risk assessments for each possible genotype. Besides, there is NO genotype that should prohibit a dog from being bred – just have to find a mate of the correct genotype to produce low risk pups. (See either the DMS genotype calculator or go to the Punnett square link at the above link.)

Remember, the risk interpretation applies to the risk of an individual dog being tested to develop clinical signs of DMS, and does not indicate the risk of that dog producing affected puppies. It is important for breeders to know and share each dog's genotype, so progress can be made in decreasing the incidence of DMS.

c. This bitch does have a low risk genotype; however, to produce a litter with all low risk puppies she should be bred to a stud with aabb genotype. Breeding her to any stud with "A" or "B" alleles, even if that dog has a low risk genotype, would mean that each pup has a chance of inheriting a moderate to high risk genotype. Each breeder must take multiple factors into each breeding and each of us may be able to accept various amounts of risk. Go to the above weblink and click on the Punnett square link or use the DMS Genotype calculator to see the various possibilities of genotypes.

d. TRUE. Although the DLA-DRB1*002:01 allele is the most common in Shelties (78% have at least one copy and 60% are homozygous for it), there are at least 2 other alternate alleles with 023:01 and 015:01 being the most common alternates. If all things are equal, and you have a choice between a stud with 002:01/002:01 and another with 002:01/023:01 or 002:01/015:01 the latter would be more desirable. Over a period of years, breeders could work toward increasing the number of dogs with 023:01 and 015:01 alleles (and any other alternates that might be found as more dogs are tested).

To put this in perspective, Collie breeders have few if any other options for the DLA as over 90% of Collies tested had DLA-DRB1*002:01/002:01.

DMS Quiz #3: The answers to this quiz are in the comment section below.

You have a bitch with 002:01/002:01Aabb genotype (low risk) and would like to breed her to a male with 002:01/023:01 AaBb (also low risk). What are the possible genotypes of the offspring and associated risk assessments?

To find the answer, go to the following webpage, http://americanshetlandsheepdogassociation.org/dermatomyos…/ Use either the "Genotype Calculator" or click on the Punnett square link....

I'll provide the answer tomorrow.

Answer to DMS practice quiz # 3:

Attached is a page from the Punnett squares posted on the ASSA website at: http://americanshetlandsheepdogassociation.org/dermatomy.../ (click on the Aabb genotype to bring up the Punnett squares).

Each pup would have the risk of inheriting one of the genotypes noted in the attachment. 12 of the possibilities are all low risk regardless of the DLA being homozygous or heterozygous. Unfortunately, each pup also runs a slight risk of inheriting moderate or high risk genotypes.

Remember, the risk interpretation applies to the risk of an individual dog being tested to develop clinical signs of DMS, and does not indicate the risk of that dog producing affected puppies.

Aabb

AaBb	Ab	Ab	ab	ab
AB	AABb	AABb	AaBb	AaBb
Ab	AAbb	AAbb	Aabb	Aabb
aB	AaBb	AaBb	aaBb	aaBb
ab	Aabb	Aabb	aabb	aabb

2 AABb: 4 AaBb: 2 AAbb: 4 Aabb: 2 aaBb: 2 aabb

12 low risk: **4 AaBb, 4 Aabb, 2 aaBb, 2 aabb with homozygous or heterozygous *DLA-DRB1*002:01***

2-4 moderate risk: **2 AAbb with homozygous or heterozygous *DLA-DRB1*002:01***

0-2 AABb with heterozygous *DLA-DRB1*002:01*

0-2 high risk: **AABb with homozygous *DLA-DRB1*002:01***

DMS practice quiz #4: - the answers to this quiz are in the comment section below.

You have a bitch that has had several previous litters with no DMS affected pups. Unfortunately, in her most recent litter of 4, 2 of the pups were affected with DMS. Which of the following is/are TRUE?

a) Obviously, this is the fault of the stud. Never touch him or any of his offspring again!
b) Not only should the DMS affected pups be spayed/castrated, the normal appearing littermates should be sterilized also.
c) Your bitch, like most Shelties, has some risk alleles for DMS. It is likely that the studs used in the earlier breedings had genotypes that when combined with that of your bitch resulted in each pup inheriting a low risk genotype.
d) You should have your bitch tested and urge the stud dog owner to do the same. Both the sire and dam had risk alleles and crossing those two genotypes resulted in each pup having the chance of inheriting low, moderate, or high risk genotypes.

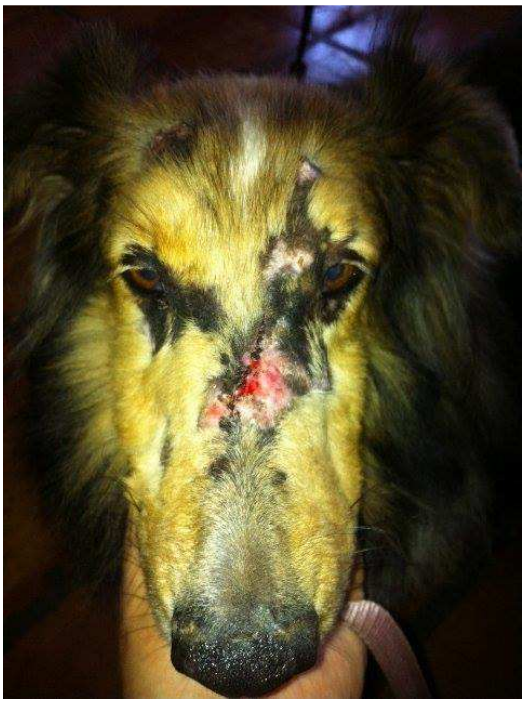
Answer to DMS practice quiz #4: C and D are TRUE.

a) FALSE. DMS is one of those diseases that cannot be caused by one parent. The affected pups must have inherited risk alleles from each parent. Take the genotype of 002:01/002:01 AaBB. This is a high-risk genotype (in the research paper 90% of dogs with this genotype had DMS). What do we know about the genotypes of the parents? Since the DLA is homozygous, we know that each parent had at least one 002:01 allele, and since the dog had BB, each parent had at least one of those. We do not know which parent contributed the “A” or the “a”. Each parent could have had low-risk genotype, 002:01/002:01 AaBb.

b) The DMS status of each pup doesn’t necessarily mean that all should be sterilized. Make that decision as you normally would. There is NO genotype that cannot be used for breeding to produce pups with low risk genotypes! If you have a dog with a high-risk genotype that otherwise has desirable qualities, you could breed the dog to one with aabb genotype and all pups would have low risk genotypes. With time (years), we can work toward decreasing the number of dogs with risk alleles while maintaining genetic diversity and desirable phenotypic traits.

c) TRUE. See above.

d) TRUE. See above.



DMS practice quiz # 5: Answers posted in the comment section below.

Okay, this exercise may not be as much "fun" as the others, but I am putting it here to encourage you to try to understand how risk assessments were developed. Below is a portion of Table 3 from the scientific article by the Clemson group. You can access a larger version at: http://americanshetlandsheepdogassociation.org/dermatomyos…/ . DO NOT BE INTIMIDATED!

In the table, C = DLA-DRB1*002:01, lower-case ...letter "c" represents any alternate allele of DLA-DRB1 such as DRB1*023:01 or DRB1*015:01. Cases = dogs with confirmed dermatomyositis. Controls = normal dogs. Penetrance = % of dogs with a particular genotype that were affected.

Using the Table below:

a. How many Shelties had the genotype aabbCC (which is seen on individual dog reports as 002:01/002:01 aabb) and how many of those developed DMS?
b. For Shelties, which was the most common genotype in which NO cases of DMS were reported?
c. What percent of Shelties with AABBCC or AABBCc genotypes developed DMS?
d. What was the risk assessment for dogs with the aabbcc genotype? Remember, cc = 023:01/023:01, 015:01/015:01, or 015:01/023:01

Answers to DMS practice quiz # 5
a. 18, one of which developed DMS. (In Collies, 44 had this genotype and 1 of those developed DMS. This is a low risk genotype. Remember, low risk does not mean no risk, but it is the best we have.
b. aaBbCC – 32 Shelties in this group. aaBbCC = 002:01/002:01 aaBb
c. 100%
d. This genotype was so rare (1 normal Collie and 1 normal Sheltie) that a risk assessment could not be calculated. As noted at the bottom of the table, risk assessments were only made for genotypes observed in at least 5 dogs.

Genotype	Collies		Shetland sheepdogs			
	Cases (n = 40)	Controls (n = 185)	Cases (n = 92)	Controls (n = 205)	Penetrance (%)	Risk*
aabbcc	0	1	0	1	-	-
aabbCc	0	5	0	18	-	low
aabbCC	1	43	1	17	-	low
Aabbcc	0	0	0	3	-	-
AabbCc	0	3	1	15	-	low
AabbCC	2	71	2	23	-	low
aaBbcc	0	0	0	5	-	low
aaBbCc	0	1	0	21	-	low
aaBbCC	0	10	0	32	-	low
AaBbcc	0	0	0	1	-	-
AaBbCc	0	0	0	14	-	low
AaBbCC	0	13	2	23	-	low
AAbbcc	1	0	0	0	-	-
AAbbCc	4	6	1	1	42	moderate
AAbbCC	15	31	7	3	39	moderate
aaBBcc	0	0	0	1	-	-
aaBBCc	0	0	0	6	-	low
aaBBCC	0	0	6	7	46	moderate
AaBBcc	0	0	2	1	-	-
AaBBCc	0	0	5	5	50	moderate
AaBBCC	3	0	23	3	90	high
AABbcc	0	0	3	0	-	-
AABbCc	0	0	2	4	33	moderate
AABbCC	11	1	11	1	92	high
AABBcc	0	0	0	0	-	-
AABBCc	0	0	7	0	100	high
AABBCC	3	0	19	0	100	high

Significant values in bold.
*Risk interpretations were only made for three-locus genotypes observed at least five times.

DMS practice quiz # 6: Answers are posted in the comment section below.

You have a gorgeous stud dog with the following genotype: DLA 002:01/015:01 aaBB. He has been bred several times before you knew his genotype. So far, no puppies have shown any signs of DMS, and several have championship points! Now, how do you handle future requests for stud service?

a. Inform bitch owners of your dog's genotype and let them decide whether or not to use your dog. After all, his gen...otype is low risk.

b. Inform the bitch owners of your dog's genotype and point out that the DLA-DRB1 015:01 is quite uncommon in the breed, and it is important to maintain that allele and increase its frequency within the breed.

c. Insist that all bitches bred to your stud be genotyped for DMS and that only bitches with low risk genotypes be bred to him.

d. To ensure that only puppies with low risk genotypes be sired by your dog, you will insist that only bitches with the following genotypes be bred to him: aabb, Aabb, AAbb. (Hint: check the Punnett squares for aaBB genotype at: http://americanshetlandsheepdogassociation.org/dermatomyos…/ .

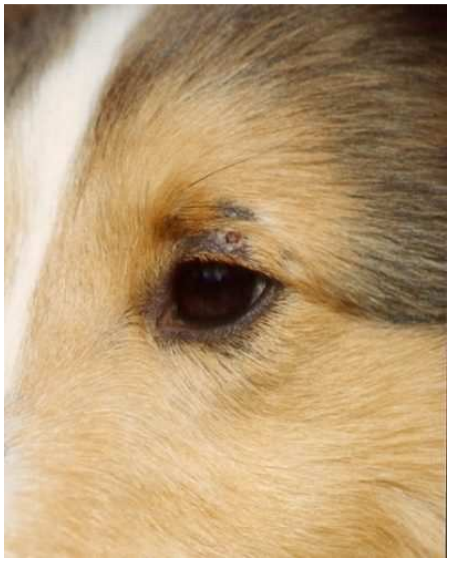
Answers to DMS practice quiz # 6:
a. In my opinion, this is an acceptable approach, especially since this is a new test and very few Shelties have been tested. Yes, the risk assessment for this dog is "low", but that applies to the likelihood of him developing DMS not to his ability to produce puppies with the disease.

b. True. The DLA-DRB1 015:01 allele is very uncommon. Only 7 of 297 Shelties tested had that allele and the breed needs more of it! BREED that dog! ☺

c. False. Insisting that only bitches with low risk genotypes be bred to the dog will NOT ensure that all pups will have low risk genotypes as bitches with low risk genotypes containing one or two "B" alleles that if bred to this male would run the risk of producing moderate or high risk genotypes. (See the DMS genotype calculator or the Punnett squares.

d. If the stud dog owner wants to ensure that his/her dog when bred would only sire pups with low risk genotypes, this would be the way to go.

Comment: I suspect that many of you have already figured out that it is best not to double up on A's or B's, so if your dog or bitch has, for example, an "A" in its genotype, it would be best to breed it to a mate with "aa", so not to double up on the "A". The above stud dog was only low risk because the DLA-DRB1 was heterozygous.



DMS practice quiz # 7: This is a series of questions.

a) I have always used the acronym DM when talking about dermatomyositis, but I now see DMS being used. What's the difference?
b) My dog's certificate from Clemson for dermatomyositis lists the DLA as 003:01/009:01; however, these numbers are not mentioned in previous test questions nor in the ASSA website. Why?
c) I submitted dermatomyositis test results to OFA, but they were not accepted. Why?
d) In the "risk interpretation" section of the DMS section of the ASSA website, what is meant by homozygous or heterozygous DLA-DRB1*002:01?

Answers to DMS practice quiz # 7:
a) For years, Sheltie owners have used the acronym DM to refer to dermatomyositis; however, in recent years, "DM" is used to refer to degenerative myelopathy which is a disease that affects the spinal cord. As a result, the acronym DMS should now be used when referring to dermatomyositis. Old habits are hard to change, but be sure to use DMS from now on.

b) The DLA numbers 003:01 and 009:01 were used in the certificates issued prior to March, 2017 and referred to DLA-DQA1. Since publication of the research, a decision was made to report a different set of numbers DLA-DRB1.

c) If your dog was tested before March, 2017, you should contact the Clemson lab for a new report to send to OFA as the DLA is being reported differently (as noted above) since publication of the research. Results will be unchanged. To receive a new certificate, contact Jacqueline Evans at jacquee@clemson.edu AND send a copy of the request to Sarah Murphy, scmurph@g.clemson.edu . Jacqueline is receiving her Ph.D. and will be moving onto to a position at NIH! Sarah is a new graduate student and will be taking over some of the correspondence previously handled by Jacqueline.

d) Homozygous DLA-DRB1*002:01 means DLA-DRB1*002:01/002:01 (The dog received the same number from each parent, so is homozygous for the 002:01 allele.)

Heterozygous DLA-DRB1*002:01 means the dog inherited 2 different numbers from each parent such as DLA-DRB1*002:01/023:01 or DLA-DRB1*002:01/015:01.

DMS practice quiz # 8: Answer posted in the comments section below.

Why do some DMS affected dogs develop lesions as young dogs while others may not develop lesions until later? (Hint: The likely answer can be found in the Summary document at http://americanshetlandsheepdogassociation.org/…/DMS-articl… .

Answer to DMS practice quiz # 8:
In dogs that developed DMS, the researchers found that there was an inverse correlation between the number of A and B risk alleles and the age of onset of the disease. “Dogs having four risk alleles developed DMS at a significantly younger median age (5 months) than did dogs with only two risk alleles (18.5 months). The complete penetrance of AABB genotypes, combined with an early age of onset, suggests that these dogs may be hypersensitive to commonplace environmental stimuli (e.g., routine puppy vaccinations).” The most common genotypes of affected dogs were AaBB followed by AAbb, AABb, and AABB, all with homozygous DLA-DRB1 of 002:01/002:01. All affected dogs had at least two risk alleles, and all but one were homozygous for at least one risk allele.

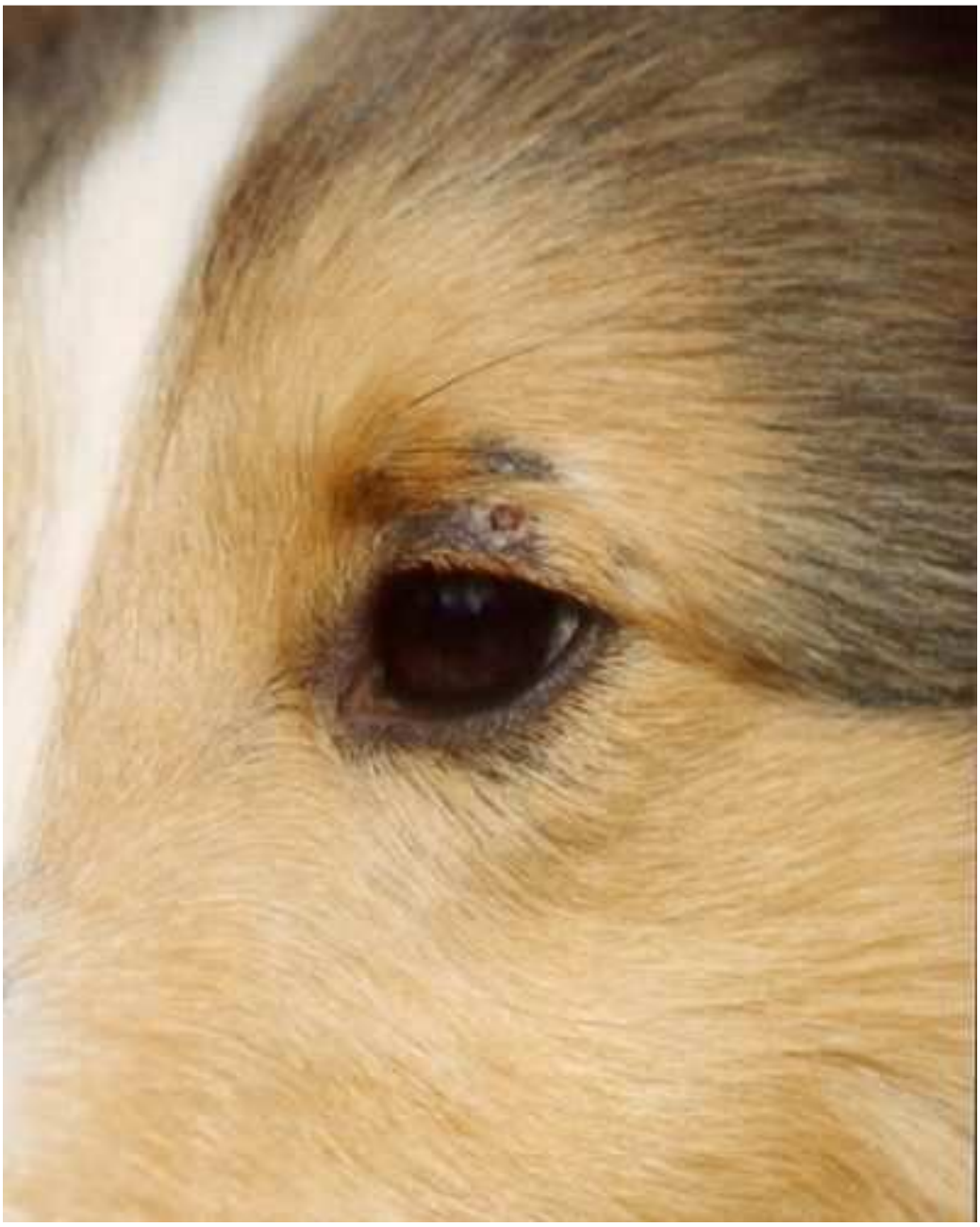
From: Evans JM, Noorai RE, Tsai KL, Starr-Moss AN, Hill CM, Anderson KJ, et al. (2017) Beyond the MHC: A canine model of dermatomyositis shows a complex pattern of genetic risk involving novel loci. PLoS Genet 13(2): e1006604. doi:10.1371/journal.pgen.1006604. http://journals.plos.org/plosgenetics/article...

DMS practice quiz #9: Answers posted in the comments section below.

You have a beautiful, young dog with the following genotype: DLA-DRB1*002:01/002:01 AaBB. This dog is exactly what you have been trying to get for years. He has won multiple specialties and finished quickly. Quite simply, he is exceptional. He had a bit of hair loss below one eye that you thought was the result of a scuffle with a kennel mate, but the hair has grown back. What is his risk for developing DMS?

Answer to DMS practice quiz #9:
The genotype, DLA-DRB1* 002:01/002:01 AaBB is high risk for the dog developing DMS lesions. In the research publication, 90% of Shelties with this genotype had confirmed DMS. Only 3 of 26 were considered to be normal.

This dog could be used in a breeding program by breeding him to bitches with aabb genotype. All puppies resulting from such matings would have low risk genotypes of aaBb or AaBb. This test allows us to maintain genetic diversity and keep desirable phenotypic qualities of dogs while decreasing the incidence of dogs with clinical signs of DMS.ow can this dog be used in a breeding program?



DMS Practice Quiz #10. Answer posted in the comments section below.

How many Shetland Sheepdog DMS test results have been entered into the OFA database?

This exercise is for those who have never used the search functions of the OFA website. Go to the OFA homepage: http://www.ofa.org/. In the upper left corner is a blue box as shown in the photo below. Click on the "Advanced Search" button. On the next page that appears, select "Shetland Sheepdog" from the breed list (next photo) then scroll down to the "Report Type" section (3rd photo) and scroll down until you find "Dermatomyositis" and highlight that. Lastly, hit the "Begin Search" button at the bottom of the page. See comment section for more information.

Answer to DMS Practice Quiz #10:

As of 5/23/17 there were 11 DMS test results of Shelties in the OFA database.

DMS Practice Quiz #11. Answer is posted in the comments section below.

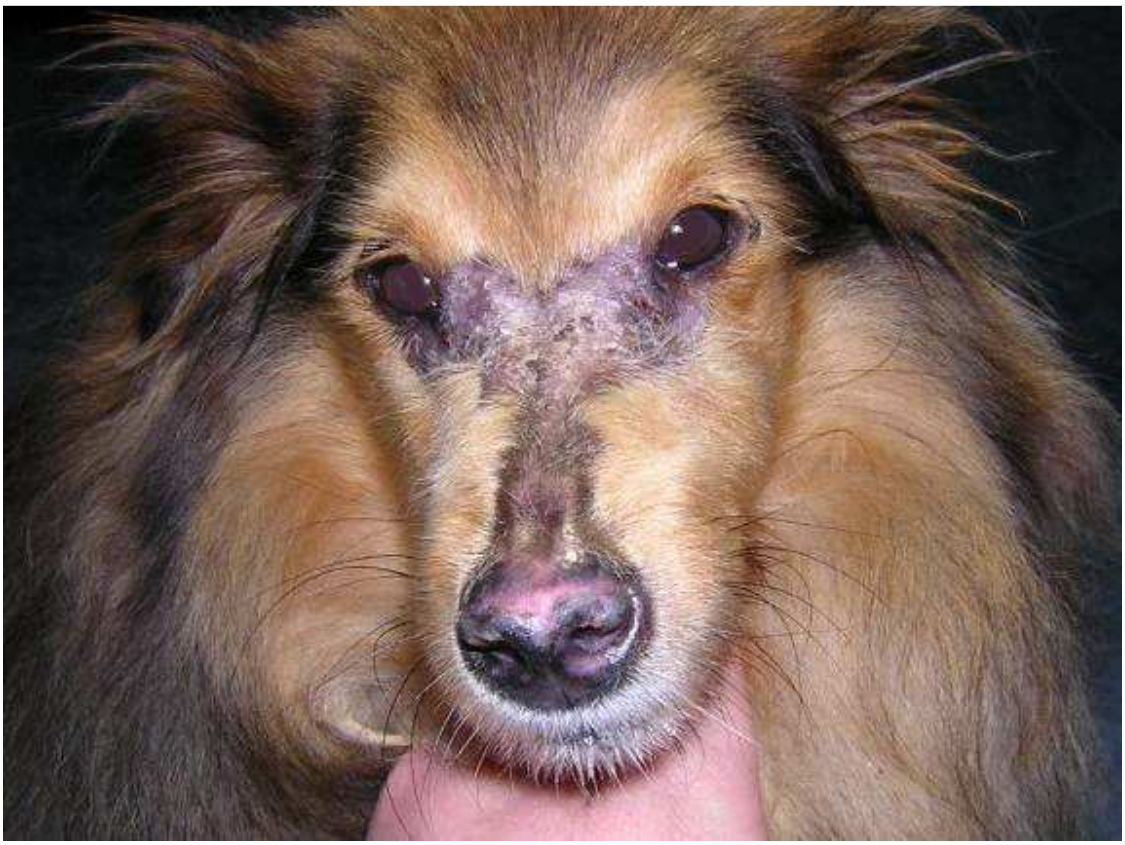
You have a dog with the following genotype, DLA-DRB1* 002:01/002:01 AaBB. Neither the sire or dam of this dog have been DNA tested for DMS. What, if anything, can you surmise about the genotype of the parents?

photo from http://www.illinoissheltierescue.com/dm.html

Answer to DMS Practice Quiz #11

• Each parent has at least one copy of DLA 002:01 allele and one copy of the "B" allele since the offspring tested has 2 copies of each (one from each parent). Therefore, the above dog is homozygous for DLA-DRB1* 002:01 and the "B" allele.

• One parent has at least one copy of the "A" allele and the other has at least one copy of the "a" allele. Since the above dog has 2 different versions of the "A" allele (Aa), it is heterozygous for it.



Summary Bullet Points for Dermatomyositis:

- A dog inherits genes from each parent. In the case of the test for dermatomyositis a dog with the genotype of DLA 002:01/002:01 Aabb means that one parent contributed 002:01 A b and the other 002:01 a b. What each parent contributed is called a haplotype (half of what makes up the offspring).
- 3 genes (DLA, A and B) act together to contribute toward the development of dermatomyositis (DMS) in Shelties and Collies.
- DLA-DRB1* 002:01, "A" and "B" are risk alleles (allele = version)
- 015:01 and 023:01 are 2 of the known alternate (good) alleles of DLA-DRB1.
- Lower case letters, "a" and "b" represent normal alleles of the A and B genes.
- Concerning the DLA – 2 different numbers such as 002:01/023:01 (heterozygous) is better than having 2 copies of 002:01 i.e., 002:01/002:01 (homozygous).
- Concerning the DLA – An owner should NOT be upset if his/her dog has 2 copies of 002:01 (ex. 002:01/002:01). About 60% of Shelties tested in the research study were homozygous for 002:01 and 78% had at least one copy. It will take years of breeding to increase the number of dogs with alternate alleles, for example, 015:01 and 023:01.
- Concerning the "A, B" genes, the goal is to gradually work toward dogs with aabb genotype.
- When breeding, try to AVOID pairings that would produce AA and or BB in the offspring.
- Use the Punnett squares or the DMS Calculator to predict possible genotypes that could result from a particular paring. See: http://americanshetlandsheepdogassociation.org/dermatomyos…/ .
- A dog with aabb genotype regardless of the DLA can be bred to any dog to produce litters in which all pups have low risk genotypes.
- Depending on the genotypes, breeding 2 dogs with low risk genotypes can produce pups with high risk genotypes.
- Except for the aabb genotype noted above, one must know the genotypes of a mating pair and use the Punnett squares (available on the ASSA website) to know the possible genotypes each pup could inherit.
- There is NO dog that cannot be used in a breeding program to produce pups with low risk genotype.
- On DMS test certificates, the "Risk" interpretation refers to the risk of the dog tested to develop clinical signs of DMS, NOT necessarily the ability of that dog to produce pups with high risk genotypes.
- DMS test results, when posted on the OFA website, can be used as one of the electives for a CHIC number. Only the genotype, not the risk interpretation is posted on the website.
- The DNA test for DMS is basically a 3-gene test which makes it costly. Think of it as having 3 MDR-1 tests done.
- e) If you have a DMS test certificate that was issued before March, 2017, GET A NEW CERTIFICATE! Request a new certificate by contacting Jacqueline Evans at jacquee@clemson.edu AND send a copy of the request to Sarah Murphy, scmurph@g.clemson.edu . Jacqueline has recently completed her Ph.D. and will be moving onto to a position at NIH! Sarah is a new graduate student and will be taking over some of the correspondence previously handled by Jacqueline. CONGRATULATIONS Jacqueline!!!!!!! ……. And THANK YOU and Dr. Clark!!!!

  Photo from: http://www.sheltierescueetn.com/page5.html

Do you have one of these??? If so, get a new certificate (like in the 2nd photo.)

If you have a DMS test certificate that was issued before March, 2017, GET A NEW CERTIFICATE! Request a new certificate by contacting Jacqueline Evans at jacquee@clemson.edu AND send a copy of the request to Sarah Murphy, scmurph@g.clemson.edu . Jacqueline is receiving her Ph.D. and will be moving onto to a position at NIH! Sarah is a new graduate student and will be taking over some of the correspondence previously handled by Jacqueline.