Price of Beauty: Exploring the Merle Gene in Cocker Spaniels

Hope A. Minga

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Abstract:

Domesticated dogs have become part of everyday life for people around the world. These dogs come in all shapes, sizes, temperaments and breeds. Some things are common across all breeds like disease, grooming needs and coat color. In terms of coat color there is a silent but beautiful threat that is unknown to most dog owners and breeders. That threat is the **merle** dilution gene mutation (Rugg & Saks, 2010). Merle dilution is a mutation in the genes of a dog that results in the dilution of the dominant coat color. Merle also results in light blue eyes and produces a unique appearance for the dog. Merle is also considered a **pleiotropic** gene, that disrupts sensory organs(eyes and ears), stomach and reproductive systems as well as other congenital and developmental incapacities(Yousha, 2006). A pleiotropic gene is gene that affects two or more unrelated traits, in this case it influences several unrelated organ systems. This makes the dog extremely marketable and profitable for pet store owners but there are many other health issues accompanied with this condition. As stewards of our pets we are responsible for being educated on topics such as merle. Having a merle dog myself, I am aware of the various limitations they experience and the lack of knowledge about the condition by pet store owners and vets. Pet store owners and breeders have a degree of responsibility as well. This paper aims to examine merle dilution, provide information and dissect the protocols,if any, implemented for breeders and store owners in terms of merle.

Introduction:

What is Merle?

To better understand the severity of merle and the health implications a further explanation of merle is required. Merle is a genetic mutation that happens in the early stages of development. It results in a coat color that is different than normal for the specific breed, lighter colored skin and usually paired with cardiovascular, skeletal, auditory, ophthalmologic and reproductive diseases and illnesses even epilepsy. It is a dominant gene so if a dam or sire possesses it their offspring will carry the gene. Double merles are dogs that are homozygous for the merle gene and usually experience the worst health issues. Heterozygous merle dogs experience less issues but still carry the gene and can pass it on to future generations.

On a microscopic level, merle is commonly attributed to the SILV locus and M locus in the dogs genes. The SILV gene is responsible for a dilution over time in non merle dogs (Clark et al, 2005). SILV plays a strong role in the expression of pigmentation and is closely related to merle expression. Genetically SILV separates itself alongside the merle gene is merle dogs, which lays claim that it is a modifier for merle genotype.

The M locus is the area in the genes directly responsible for merle but there are many instances that merle can be modified. It has recently been recently found that there are several merle alleles other than the original reported M, such as Mc, Mc+, Ma, Ma+, M, Mh (Langevin et al, 2018). This study observed 181 various dog breeds from around the world and recorded that the different alleles corresponded with different colors in merle breeds. One major cause of this new found information has been the genetic discovery that sperm cells can affect the merle mutation and cause various phenotypes to present themselves. There is also a phenomenon of

mosaicism within the alleles which causes the alleles to all be mixed in varying arrangements (Langevin et al, 2018). All of these contribute to the expression of merle in dogs, it can affect the coloring as well as the degree of health impairments the dog faces. It has not yet been definitively shown which allele results in which coloring but the fact that this breakthrough has been made is amazing and great for the scientific community as well as breeders.

However some of the alleles have been linked to certain coat types. For instance Ma and Ma+ are linked to a diluted brownish hue. While Mh is associated with merle coating with areas deleted to white or tweed and M is the classic coat color of merle. Mc and Mc+ aren't associated with a coat color but instead a solid coat color as well as cryptic merles (Langevin et al,2018). Figure 1 shows the relationship between the variants of M genes, the main difference being the length of the lengths of the DNA, it is clear how through this figure that merle is complex and genetically so similar but phenotypically so different. Figure 2 shows the frequency of each allele as recorded by Langevin et al. We can surmise that the m allele is the most prevalent, meaning that most of the merle dogs studied were heterozygous merle dogs. The more information on merle genetics the better vets and lab technicians can determine which dogs have merle and maybe even what illnesses if any they might experience.

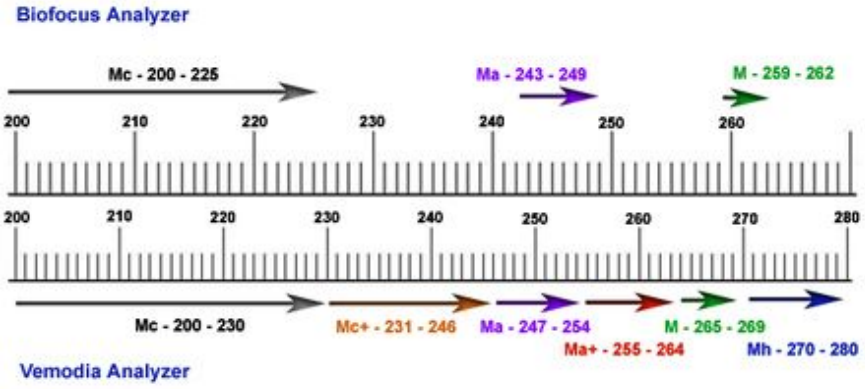

Figure 1. Visual representation of various merle alleles

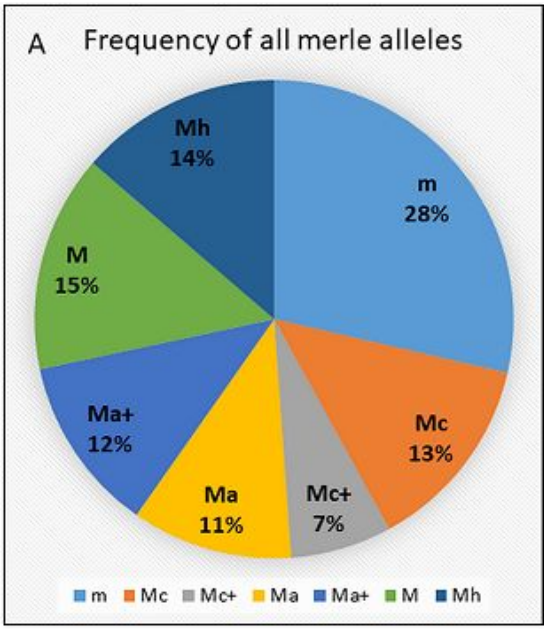

Figure 2. Demonstration of the frequency of each merle allele as presented by Langevin et al.

Merle mutation causes lasting effects to dogs both physically, in the their coat color and appearance, and internally, blood disorders such as **neutropenia,** the source of merle mutation can be pinpointed in the DNA (Langevin et al, 2018). Neutropenia is an abnormality in the blood that makes the dog more susceptible to infection, which can lead to death. A complete linkage map of dog genome, as well as disease and evolutionary pathways, was produced as recently as 2010 (Wong, Rue,et al, 2010). More recently a mutation in the alleles of several types of dogs has been studied and mapped as well.

This mutation results in a merle coat, light eyes, nose and/or pads (Figure 1,Rugg & Saks, 2010). Merle genetically only affects eumelanin, which means that it only dilutes black (Figure 2), liver(Figure 1) and blue any other colors will remain unaffected by the merle gene. This dilution occurs in the skin, coat and eyes which results in the drastic physical difference

between merle dogs nad non merle dogs. The result is one blue eye or both, light pink skin and pads. These lighter colored eyes, nose, pad and skin results in extreme sensitivity to sunlight, making merle dogs prone to sunburn and skin damage and sun sensitivity.

Figure 3. Liver (Red) merle Australian Shepherd with Heterochromia iridis

Whether the canine has one or more **phenotypes** is dependent on several things, mainly whether they are **heterozygous** or **homozygous** for the mutation.A phenotype is the expression of traits, such as coat color, eye color, size and temperament in terms of dogs. When a gene has two different alleles it is known as heterozygous (Mm), when both alleles match it is referred to as homozygous also known as double merle (MM). Even though merle coat pattern is recognized by the **American Kennel Club** for many breeds such as Dachshund, Collie's, Great Danes, Australian Shepherd and the Shetland Sheepdog, the focus of this research is Cocker Spaniels.

The American Kennel Club is a registry for purebred dog and a company that houses all knowledge dog and breed related. Since Cocker Spaniels aren't a recognized breed for merle most of the research uses other breeds of dogs. Nonetheless all the information is still relevant to the issue. The American Kennel Club is a registry for purebred dog and a company that houses all knowledge dog and breed related.

The Cocker Spaniel is a well known breed with two main divisions, English and American Cocker Spaniels. The American and English cocker spaniels have marked differences in appearance as well as size and temperament. The cocker spaniel breed is known for being a quiet breed with rare barking, as well as being easy to train due to their desire to please. The English cockers spaniel is slightly taller than the American cocker spaniel and has a longer face and snout and averages about thirty pounds (McKinney). There are many normal coat patterns among cocker spaniels: black, red, liver, golden, tan, orange, red, buff and many others; merle is a dilution of these colors resulting in lighter shades as well as white and grey (Gormish). Merle coat pattern is also accompanied by many diseases, deformities and auditory and ophthalmologic defects (Strain et al, 2009).

Figure 4. Merle Cocker Spaniel with starburst pupils.

Statement of research problem:

There are many different types of merle based on the dominant color scheme of the coat (Clark et al, 2005). Some would consider these differing coat patterns to be exotic or unique making them desirable. This desirability can increase the cost of these pets and the value they can possess for breeders and sellers. Merle dogs experience varying levels of health problems, from simple eye issues to total blindness and seizures(Rugg and Saks, 2010).Merle dogs can experience an array of symptoms and many times suffer because of the issues they face. Many merle dogs are also born with one eye or no eyes (**Anophthalmia)** and it is unknown how many of these dogs have been euthanized or abandoned.

There needs to be more education and safeguards to prevent further breeding. Is there a way to educate breeders and buyers about merle patterning and potential risks and are there policies in place to safeguard this abnormality? In this paper I aim to build upon quantitative research to prove that merle breeding should be regulated and if not the public needs to be educated about merle gene mutation and how it can affect their dogs. Merle gene mutation is experienced by dogs all around the world and it is time that someone took some measure to help spread word about it.

Background:

Merle dogs have long been described as “exotic” “unique” “gorgeous” as so on but until recently science had not made the connection between merle and the various health issues associated with it. There is still more conditions that are being studied and linked to merle genetic mutation. Merle gene mutation has become a massive topic among scientists. Some of the major researchers are George M. Strain who has extensively researched deafness in merle

Great Danes, many would consider his work to be the beginning of this call to action in terms of merle gene mutation. Another major researcher is Leigh Anne Clarke who has contributed to countless research papers regarding the location and cause of the gene mutation in the DNA of dogs and in the deafness of merle dogs. Both of these researchers aim to inform readers about any and all information related to merle, mainly information not before recorded. Dr. Audrey Webb is a veterinarian that has also studied hearing loss and testing extensively and aids in the next steps for merle dog owners. This paper will add their research together to present a cogent set of information that gives the audience the opportunity to make informed decisions when adopting or purchasing dogs. All of my research has proven my thesis that merle is not a sustainable mutation, should not be bred for sale and the sale should be regulated. Even though the researchers show that merle deafness and other symptoms aren't as prevalent in merle dogs as in double merles nonetheless the facts don't lie.

Discussion:

A closer look at merle phenotypes: There are many different types of merle such as: black, blue, slate, lilac, light, heavy, tipped sable, brindle, harlequin and tweed. These differences are determined by the predominant color expressed in the coat of the dog. There are also many ophthalmologic and auditory deformities than can accompany a merle dog. Some scientists hypothesize that these developmental issues can be linked to the process by which a merle genotype is created and in that creation a removal of another gene occurs (Cordaux & Batzer, 2006).

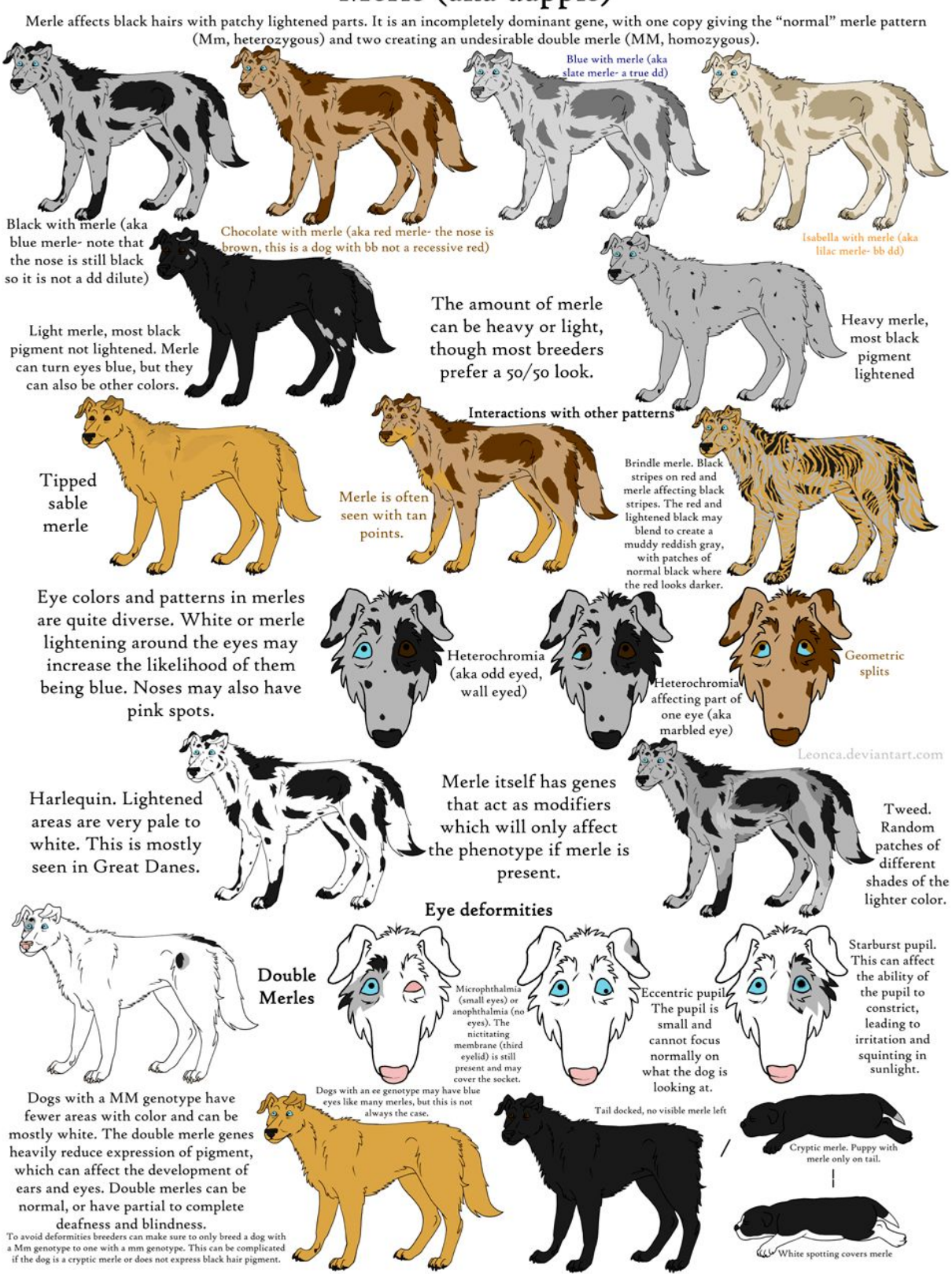

Figure 5. Complete diagram explaining merle phenotypes.

A closer look at merle phenotypes: There are many different types of merle such as: black, blue, slate, lilac, light, heavy, tipped sable, brindle, harlequin and tweed. These differences are determined by the predominant color expressed in the coat of the dog. There are also many ophthalmologic and auditory deformities than can accompany a merle dog. Some scientists hypothesize that these developmental issues can be linked to the process by which a merle genotype is created and in that creation a removal of another gene occurs (Cordaux & Batzer, 2006).

Some of the possible health issues are **bilateral microphthalmia**, auditory and sight impairments, seizures, eye deformities, **neutropenia** which can lead to serious infections, **alopecia**, as well as skeletal, cardiac and reproductive system issues (Clark et al, 2005). Some dogs are rendered completely blind or deaf, and sometimes both. Although studies have been conducted that show the prevalence of deafness to be low amongst homozygous and heterozygous merle dogs, (Strain, Clark, Wahl, Turner & Murphy, 2009) those studies did not include Cocker Spaniels. Merle dogs can also possess the mutation but show no overt phenotypes, these are known as ghost or **cryptic merles** and can still pass on the mutation to offspring (Kaelin & Barsh, 2013).

This is one of the many reasons breeding merle and merle is highly frowned upon. It was believed that breeding heterozygous merle dogs with non-merle dogs would result in offspring without the merle gene. This has been disproven (Figure 3) and there is currently a genetic test in North America through IDEXX Reference Laboratories that can confirm that the resulting offspring isn't a cryptic merle or a merle at all (Rugg, Saks, 2010).

We can see from figure three that the breeding of a merle and non merle results in fifty percent merle offspring and merle and merle breeding results in fifty percent merle offspring, twenty five percent double merle and twenty five percent non merle. This shows that merle gene is dominant and cannot be breeded out. This has been further proven by the discovery that merle mutation doesn't occur in just one area. There are several areas in the DNA that can cause a dog to become merle (Langevin, et al 2018). Langevin et al maps out the gene mutation as being Mc to Mh whereas previously merle mutation was believed to occur only at the M locus(Clark et al,2005) and occasionally the H locus resulting in harlequin coat pattern.

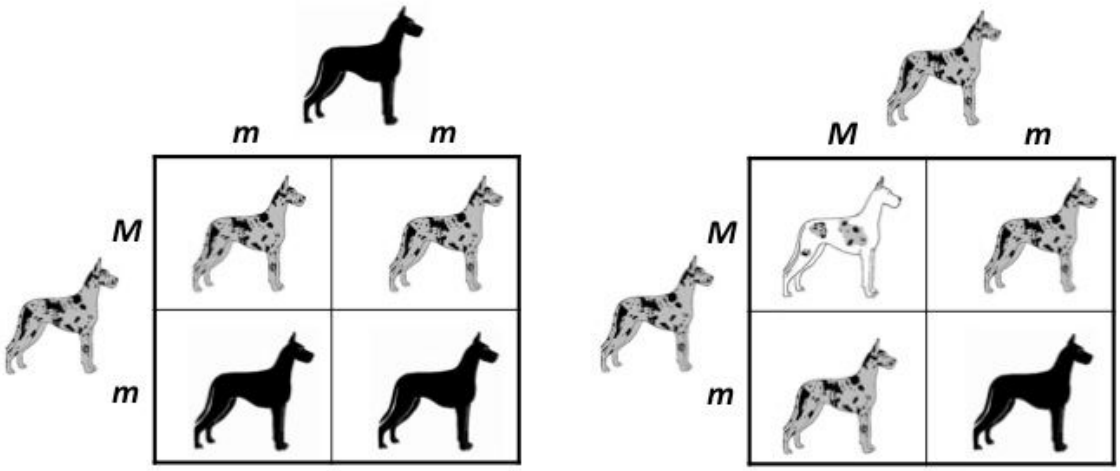

Figure 6. Punnett Square of Merle (Mm) breeding with non merle (mm) and breeding of two merle(MmxMm)

Some of the possible health issues are **bilateral microphthalmia (** figure 4), auditory and sight impairments, seizures, eye deformities, **neutropenia**, **alopecia**, as well as skeletal,

cardiac and reproductive system issues (Clark et al, 2005). Alopecia is the loss of hair where hair should be present, or in some extreme cases, complete baldness. Some dogs are rendered completely blind or deaf, and sometimes both(Figure 2). Although studies have been conducted that show the prevalence of deafness to be low amongst homozygous and heterozygous merle dogs, (Strain, Clark, Wahl, Turner & Murphy, 2009) those studies did not include Cocker Spaniels. Merle dogs can also possess the mutation but show no overt phenotypes, these are known as ghost or **cryptic merles** and can still pass on the mutation to offspring (Kaelin & Barsh, 2013).

Auditory and Ophthalmologic deformities

Effects to the auditory and ophthalmologic systems can vary greatly in pronunciation and magnitude. Out of one hundred and fifty-three merle dogs tested in a study only 4.6% were unilaterally and bilaterally deaf (Strain et al, 2009). Seemingly small percentages but upon further inspection heterozygous merle (Mm) were 2.7% unilaterally deaf and only 0.9% bilaterally deaf. In comparison, double merle or homozygous merle (MM) were 10% unilaterally deaf and 15% bilaterally deaf (Strain et al, 2009). This shows a clear trend amongst homozygous merle to be more susceptible to deafness.

Along with deafness, merle dogs can experience actual deformities in the shape of their pupil as well as the size of their eye. Some of these deformities include eccentric pupils which produce a cross-eyed effect and prevent the dog from focusing very well. Another is starburst pupil which prevents the eye from constricting which causes irritation, sensitivity to light and squinting or eye watering in high light conditions. Dogs with merle mutation can also experience bilateral or unilateral microphthalmia as well as **anophthalmia**. **Microphthalmia** makes the

eyes abnormally small and anophthalmia is the lack of one or both eyes. Another ophthalmologic issue merle dogs experience, is **heterochromia iridis.** Heterochromia iridis is when two different eye colors are present, this is especially prevalent among australian shepherds. Even though there is no health effects from this condition it is one of the characteristics that make merle dogs desirable and sought after.

One other major disadvantage for merle dogs is the pigmentation of their skin which is often a light pink which is prone to sunburn and sun damage. This is not even half of the possible defects associated with this genetic mutation that some consider the most beautiful coat pattern(O'Dea, 2014).

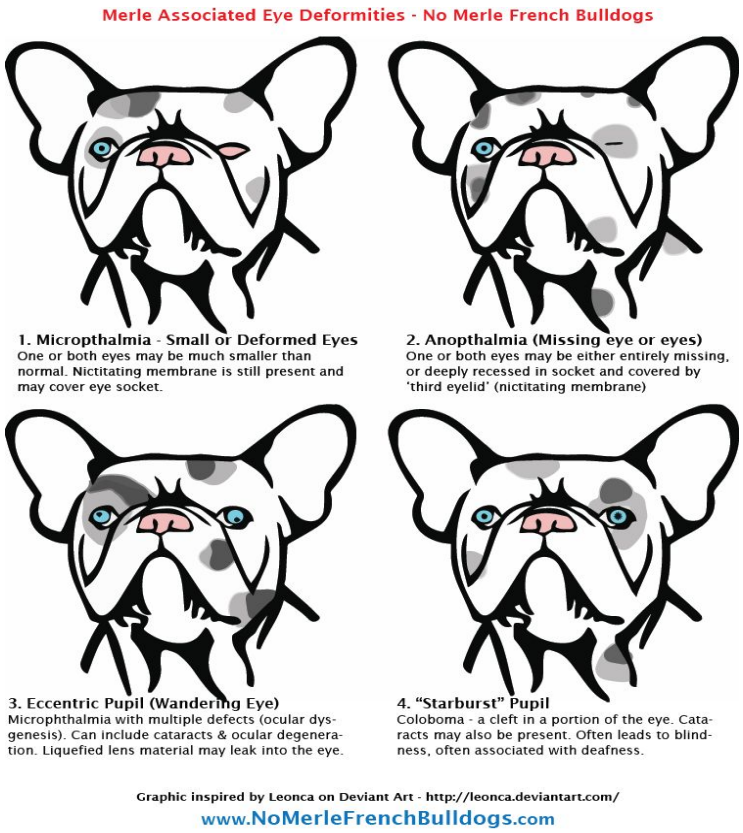

Figure 7. Eye abnormalities in merle dogs.

Conclusion:

Currently in the U.S. there is no restriction to merle breeding. In the United Kingdom however they have been to put strict regulation on merle breeding and have made the registering of homozygous dogs not allowed. They also forbade the breeding of two merles together to try to prevent merle offspring. They have also placed heavy restriction to the chihuahua breed and will not allow the registration of any chihuahua merle colored dog. Their aim is to erase merle from the chihuahua breed, because it was introduced through breeding and doesn't occur naturally in chihuahuas. While doing all this they still allow the registration of heterozygous merle dogs which isn't as responsible as banning them all. All that being said the American Kennel Club is quite behind when it comes to regulating merle registration or education. They do however have a canine health foundation that funds research to improve the health of dogs and research topics like merle more thoroughly. In this sense they are making an effort to help and educate.

Even though there are no regulation by AKC most states don't have regulations either. In order to sell dogs and cats in NYC a person needs only to get a NYC Pet Shop (D) Cats and Dogs" permit and a Pet Dealer license. The costs total to a few hundred dollars and need to be renewed every two years. The owner also has to provide the dog or cat with a microchip, spay or neuter before sale and a full health report detailing sire and dam, as well as any health problems. Possible downfalls of these requirements are that not all states may require spay and neuter before sale and if breeders or vets don't know about merle they wouldn't list it in health problems. This is a step in the right direction at least in NYC the amount of merle puppies born is somewhat limited.

Steps for owners:

Even though there aren't a lot of regulations or requirements in place for pet shop owners there are a lot of resources available to dog owners. There is the IDEXX DNA test to determine whether or not a dog is merle. This test is available around the world and is vital in managing merle dogs by allowing owners to know what to expect and begin getting their dog thoroughly examined.

There is also an eye test that tests for genetic eye diseases in the dog. This exam is done by OFA and reported to their Companion Animal Eye Registry (CAER) this is an attempt to provide information to breeders and owners about possible genetic eye diseases so that the owners can make informed decisions when breeding dogs. The exam takes 30 to 40 minutes and is done by a veterinarian ophthalmologist and is painless to the dog. The detailed results of the test are stored by the vet put into the CAER database and given to the owner. The test costs about fifty dollars. This test is vital for merle dog owners because in some cases, depending on the age of the dog, the eye deformity or disease may not be noticeable to the naked eye. The test is also great for general knowledge for any dog owner. The more you know about your dog the better you can care for them.

There is also a hearing test that dogs can take called BAER which stands for the Brainstem Auditory Evoked Response test. This tests use the brain stem by which they can see activity in the brain once a sound is played. This activity is a reaction to the sound and alerts them to the dogs ability to hear the sound(Webb,2009). If the dog's brain activity shows no reaction that dog can be labeled deaf unilaterally(Figure 5) or bilaterally(both ears). This test determines the hearing level of the dog in the same way doctors test children and adults. It costs

about seventy five dollars for the exam and the results. The test can be obtained at several testing sites around the continental US. The main drawbacks of this test is that it doesn't test within all the hearing levels of a dog just encompassing the levels of a human so the results can be skewed. The dog may test deaf but still be able to hear high pitched sounds above the human hearing level.

Figure 2

Source: *Webb, Aubrey A, Brainstem auditory evoked responses (BAERs) from a 2 month old Australian cattle dog with unilateral inherited coat color-related deafness, Brainstem auditory evoked response (BAER) testing in animals, The Canadian Veterinary Journal 50.3, 2009, 317, Web, Photo.*

Figure 8. BAER results from a dog with inherited coat color deafness perhaps merle.

Managing Life with a Merle dog with disabilities

There is also a nonprofit organization called Keller's Cause that works to educate owners and breeders about the risks of breeding double merle and how to train double merles with

hearing or seeing impairments. The founders both have double merle dogs, one that is blind and deaf and one that is deaf. They have a youtube page and release videos to help other merle owners learn how to better train and communicate with their impaired merle dogs. They also attend expo and trade shows to further educate and demonstrate the lesser known traits of merle dogs (rex specs,2017). Technology exists to train dogs that are blind, deaf or both and that is vibration collars, some trainers even teach deaf dogs sign language. There is also special goggles formulated to protect dog eyes from UV damage which is great for merle dogs and have a more comfortable fit than traditional dog goggles. These goggles are also vet approved. They are quite pricey around seventy dollars before tax and shipping but worth it if you have a light sensitive dog. There is a lot of technology and equipment available to help communicate with dogs with these impairments and disabilities and even though these dogs have these limitations they are still very smart and capable of the same or more as healthy dogs.

Figure 9. Rex Specs

I hope that through this research the people who read it will question every aspect of a dog before purchasing it, to have more information and be able to give the dog the best life that they can. I don't wish for people not to purchase merle dogs, every dog deserves a loving home and in that home should be people who know how to take care of the dog. They also should know what conditions warrant restriction to breeding to help stop the spread and suffering of future merle dogs.

The vibration collar acts as a call to the dog and notifies the dog to wait for a command. Usually an owner can train the dog to accept certain affirmations, such as a thumbs up, finger wag and so forth. Even though the dog may be deaf or blind they can hone their other senses and have the same capabilities as hearing or seeing dogs (Messer, year unknown). As well as with blind dogs there are many methods and technology available to help train and better equip yourself and your dog for urban life while impaired. There is clickers to train dogs with as well the scenting method. Which involves scenting tables and corners to allow the dog to learn where everything is, the vibration collar can also be used with blind dogs. Even something as rudimentary as dog whistles can be very useful. Knowing all of these methods and technology available it is said to know that most breeders still euthanize dogs born blind or deaf, feeling they have no chance to a normal life (Messer)

Call for Further Research

Since a lot of my research material is new there are some limitations to the research. As further information is acquired for merle dogs and merle genetics, there will continue to be advancements in genetic testing and determinations of merle and cryptic merle dogs. There is still a lot of missed merle diagnoses, so there may be merle dogs breeding with the potential to

pass on the gene. As seen in Langevin et al study from earlier this year there are some genetic material consistent among merle dogs not seen in non merle dogs which can be a determinant for merle but have no current testing available.

Hopefully as science progresses there will be continued advancements for the protection and care for merle dogs and then eventually regulations and implementations for pet store owners and breeders. This will allow for better monitoring and limiting of the spread of the genes and ailments. I am hopeful that once science fully maps out merle and produces accurate testing that lawmakers will help crack down on merle production and sale.

There is a lot that can be done by everyday people, you don't have to be a scientist to educate yourself on issues that can impact your life. Merle dogs are worldwide in larger numbers than many estimate, so it is our duty and the duty of people around the world to learn about merle and other conditions like merle. Being a proud owner of a heterozygous merle dog I will continue to keep myself abreast with the latest advancements to ensure the continued health of my dog.

Figure 10. A blind and a deaf double merle Australian Shepherd pair.

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Figure 2: retrieved from Langevin et al article (13)

Figure 3: retrieved from:

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Figure 4. Personal Photograph

Figure 5. retrieved from:

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Figure 8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2643461/

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Figure 10: retrieved from: https://www.rexspecs.com/blogs/news/kellers-cause