

An Overview of Equine Multiple Congenital Ocular Anomalies (MCOA)

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Introduction

Multiple Congenital Ocular Anomalies (MCOA, formerly called Anterior Segment Dysgenesis (ASD)) is an inherited eye disease of horses. The disease is congenital (present at birth) and generally does not progress in severity over the lifespan of an affected horse. Two types of ocular changes occur in association with the MCOA disease complex: 1) fluid-filled cysts that are present on the posterior iris, peripheral retina, or ciliary body, which is a structure within the eye that is located just behind the iris, and 2) cysts in combination with other ocular defects affecting the cornea, iris, lens, and/or retina (for details of the ocular defects, see Ramsey et al, 1999a). The two phenotypes are termed “cyst” and “MCOA,” respectively. Thorough ocular examination by a veterinary ophthalmologist or veterinarian familiar with clinical signs associated with this disease is required to diagnose cysts or MCOA. Cysts in particular can be very difficult to see and may require use of specialized equipment by a veterinary ophthalmologist to discern.

Nomenclature

The acronym MCOA replaced the acronym ASD (Anterior Segment Dysgenesis), which was used formerly to denote this constellation of congenital eye abnormalities in horses. The reason MCOA was selected to replace ASD is because ASD was a poorly descriptive title, as there are many different eye syndromes in both human and veterinary medicine that fall under the general category of dysgenesis (abnormal formation) of the anterior segment of the eye, which is composed of the cornea, iris, ciliary body, and lens. Therefore, the term ASD has been orphaned and replaced with MCOA.

Impact of ocular defects

The presence of MCOA-related cysts in affected horses is minimally detrimental, as cysts are not painful and do not affect vision. In contrast, MCOA-related defects in the cornea or lens may decrease visual acuity, but like cysts are not painful. The changes associated with MCOA that have the potential to cause problems with vision are corneal abnormalities and cataracts. Cataracts attributable to MCOA are present at birth and are essentially static, that is, the cataracts do not change with advancing age or changes may progress very slowly. Vision is rarely affected in MCOA horses with cataracts. It is important to realize that cataracts can form from non-

Box 1. Definitions

Anomalies: Deviations from normal.

Allele: The different forms of a gene (with designations such as “N” or “M”). In animals, one allele is inherited from each parent.

Congenital: Present at birth

Genotype: The genetic constitution of an individual. The pair of alleles (such as “NM”) of a gene that encodes for a specific trait.

Homozygous: The same form of allele is inherited from both parents (e.g., “MM”)

Heterozygous: Different forms of an allele are inherited from each parent (e.g., “NM”)

Mutant: A genetic defect with deleterious effects.

Ocular: Pertaining to the eye.

Phenotype: Observable characteristics of an individual that are determined by its genotype and environmental influences.

genetic causes, such as secondary to inflammation inside the eyes or trauma, and these types of cataracts frequently do progress and have the potential to impair vision. The second MCOA abnormality that can impair vision is cornea globosa, a condition in which the curvature of the cornea is excessive, which causes the eyes to appear to protrude excessively (colloquially referred to as “pop-eyes”). MCOA foals that have cornea globosa do have optical differences that result in severe near-sightedness (the foal sees clearly up close, but has blurry and very magnified distance vision). Based on results of our previous research (Ramsey et al, 1999b), MCOA foals with cornea globosa develop normal optics after reaching 1 year of age; i.e., the optics of the eye of a MCOA foal with cornea globosa may be poor during the first year of life, but once the foal matures to one year of age, this horse’s vision is no different from the vision in a horse that does not have cornea globosa.

Inheritance

Pedigree analysis of large numbers of horses with cysts or MCOA defects indicates that a single major gene underlies inheritance of this disease (Ewart et al, 2000). Further genetic mapping studies have determined that the gene causing MCOA is located on equine chromosome 6 between nucleotide positions 73,658,168 and 73,835,084 (Andersson et al, 2008; Andersson et al, 2011a). While the precise identity of this gene has not yet been conclusively determined, the inheritance pattern of the disease is clear. Specifically, the inheritance of a single mutant (defective) copy of the causative gene results in the cyst phenotype, whereas, when mutant forms of the gene are inherited from both parents (two defective copies), the multiple ocular defects characteristic of MCOA occurs. Thus, cysts and MCOA are gradations of different levels of severity of the same disease. Indeed, the cyst phenotype is essentially the “carrier” phenotype for MCOA. Genetically, cyst-affected horses can be considered MCOA carriers, and are referred to hereafter as “cyst/carriers.”

In addition to a major gene causing MCOA, a small number of horses may have one or a few “minor” genes that modify the disease expression, potentially masking the presence of the mutant major gene. The search for the major gene causing MCOA is ongoing.

Association with coat color

Ciliary body cysts and MCOA have been found in horse breeds that have the silver dapple, known as “chocolate,” coat color. Specifically, Rocky Mountain Horses, Kentucky Mountain Horses, American Miniature Horses, and Icelandics have been reported to be affected with MCOA (Andersson et al, 2011a; Andersson et al, 2011b; Kaps and Spiess, 2010; Grahn et al, 2008; Ewart et al, 2000; Ramsey et al, 1999a) and other breeds, while not yet reported in the veterinary literature, are likely to have it as well. The silver dapple (chocolate) coat color is determined by the *PMEL17* gene (Brunberg et al, 2006), which causes a dilution of the black coat color pigment, thus creating the chocolate brown coloration. The *PMEL17* gene is located on equine chromosome 6 in the same region to which the gene causing MCOA maps. Because genes that are physically near to one another tend to be inherited together, the *PMEL17* and MCOA-causing genes are genetically “linked” and thus the rate of MCOA and cysts is highest in chocolate-colored horses. Despite this linkage, the disease does occur in horses of other colors, and not all chocolate horses are affected.

Breeding considerations

Horses and other animals contain two copies of each gene, termed “alleles,” one from each parent. Likewise, each parent contributes one of its two alleles to each offspring. The likelihood of inheriting one allele or the other from a parent is random and since there are only two possible alleles at each locus, the probability of inheriting either one is 50%, like the probability of obtaining “heads” on a coin toss. When these alleles are the same (e.g., NN or MM) they are termed “homozygous.” When a horse has two different alleles at a locus (e.g., NM), it is termed “heterozygous.”

The Punnett square (Table 1) displays the likely phenotypic outcomes for any single gene trait. In Table 1 the genotype of unaffected horses at the MCOA locus is represented by NN, cyst or carrier horses represented by NM, and MCOA-affected horses represented by MM.

The only type of allele carried by, and thus inherited from, an MCOA-affected parent is the mutant allele, M; therefore, all of the offspring of an MCOA-affected horse will be cyst carriers (NM) if bred to an unaffected (NN) horse. While it is predicted that half the time a cyst/carrier horse will transmit a normal allele (N) and half it will transmit a mutant allele (M),

like the coin toss, the results are often not precisely 50:50 heads vs. tails or N vs. M.

Acknowledging the potential for slight variability, it is still the case that MCOA-affected horses bred to cyst/carrier horses will never produce genetically unaffected horses, as approximately half the offspring will be cyst/carriers (NM) and half will be MCOA-affected (MM). Breeding cyst/carriers (NM) to unaffected (NN) horses will produce approximately half unaffected (NN) and half cyst/carrier (NM) offspring.

With this knowledge, informed breeding decisions can be made. The first step toward a breeding decision is to establish a goal. With regard to MCOA, it is recommended that the goal be to avoid generating foals with the complete MCOA phenotype. To achieve this goal, MCOA horses should only be bred to unaffected horses.

A reasonable secondary goal may be to reduce the prevalence of cyst/carrier horses in the breeding population. However, until the genetics of coat color can be untangled from the genetics of MCOA, it is not clear whether the chocolate (silver dapple) coat color can be readily maintained when selecting against cyst/carrier animals. Despite this current uncertainty, the goal of avoiding the generation of MCOA-affected horses can still be achieved while using cyst/carrier horses in a breeding program, especially if they are bred to unaffected horses. Fortunately, the cyst phenotype is an observable marker for the carrier state of MCOA, thus informed breeding decisions can be made in the absence of a genetic test. However, we have observed the occasional horse that appears to have incomplete penetrance of the cyst or MCOA phenotype. These are horses that have no observable ocular defects but whose parents have

Table 1. Punnett square of phenotype probabilities

	Unaffected parent (NN)	Cyst/carrier parent (NM)
MCOA-affected parent (MM)	0% unaffected (NN) 100% cyst/carrier (NM) 0% MCOA-affected (MM)	0% unaffected (NN) 50% cyst/carrier (NM) 50% MCOA-affected (MM)
Cyst/carrier parent (NM)	50% unaffected (NN) 50% cyst/carrier (NM) 0% MCOA-affected (MM)	25% unaffected (NN) 50% cyst/carrier (NM) 25% MCOA-affected (MM)

N = Normal allele, M = Mutant allele

MCOA and whose offspring have cysts or MCOA. These horses are very likely to be carriers of the MCOA mutant allele, but did not express the ocular phenotype themselves. These are rare, and would require a genetic test (when available) or pedigree/breeding analysis to identify.

Current research

Working with researchers at Uppsala University in Sweden, we are trying to determine the specific gene that causes ocular cysts and MCOA in horses. Genetic sequencing of the MCOA locus to identify DNA variation between affected and unaffected horses is underway. Once the gene has been identified, a genetic test will be developed and studies will continue in order to determine the molecular mechanism by which this condition occurs.

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