The Challenge of Alpha-Mannosidosis in Murray Grey Cattle

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What is Alpha - Mannosidosis?

Mannosidosis is a lysosomal storage disease that results from a defect in glycoprotein metabolism and affects Angus and Angus-related breeds of cattle, such as Murray Greys. The congenital disease is caused by an inherited deficiency of the lysosomal enzyme alpha-mannosidase, and is inherited in an autosomal recessive manner. (https://pubmed.ncbi.nlm.nih.gov/4082380/#:~:text=Mannosidosis%20is%20a%20lysosomal%20storage,Murray%20greys%2C%20and%20the%20cat.)

Although Alpha -Mannosidosis (MA) is one of the oldest known genetic defects to be identified in Angus and Angus-derived cattle, awareness of the defect has been very limited among cattle producers. The knowledge of MA is largely due to the efforts of Angus Australia, as they met an MA outbreak vigorously and have had good results in eliminating the mutation from their population. That eradication process was initiated in 1980 as the result of several Australian animals being diagnosed with MA. The development of a DNA test for MA in 1997 provided Angus Australia with an accurate tool for identification of carrier animals. Although Australia has the most experience with MA, it has been documented in other countries, including an American case in the late 1970s. (While only 1 case was documented in the US, there is eye-witness testimony of several other cases. {Personal Correspondence}) Tests for the detection of animals heterozygous for a-mannosidosis were undertaken on samples taken from 34,209 cattle registered with the Angus Society of Australia. Results indicated 1,836 (5.4%) of the animals were heterozygotes (affected with the disease). Heterozygotes were detected in 214 (51%) of the herds examined. (Aust. vet. J. 60: 135-13 May 1983)

New Zealand moved first to eradicate alpha-mannosidosis. The New Zealand mannosidosis control program, based on testing for heterozygous individuals, was the first inherited disease-control program implemented in a national population of animals to be reported (Jolly 1978). Initiated in 1972 and completed in 1982, it has effectively controlled the economically important mannosidosis disease of cattle in the island nation. (https://www.tandfonline.com/doi/abs/10.1080/00480169.2002.36277?journalCode=tnzv20)

How is the disease presented?

Affected calves may be born alive with no physical deformities. Prior to reaching sexual maturity, affected animals show severe, progressive neurological disease characterized by tremors of the head, loss of muscle coordination and aggression when disturbed. The net effect is eventual death. Along with the afore mentioned symptoms there may also be abortions and prenatal death. (https://www.merckvetmanual.com/nervous-system/congenital-and-inherited-anomalies-of-the-nervous-system/congenital-and-inherited-multifocal-disorders-of-the-nervous-system-in-animals) It is possible for alpha-mannosidosis to remain undetected in a herd for years if abortion and prenatal death are the only symptom.

What is the inheritance pattern of Alpha -Mannosidosis?

The inheritance of MA is classified as simple recessive. Thus, only animals possessing two copies of the MA mutation will exhibit the genetic defect. Carrier animals (those animals possessing one copy of the MA mutation) will appear normal but, when mated to another carrier animal, will produce an MA-affected animal 25% of the time. (https://redangus.org/wp-content/uploads/2018/02/Alpha-Mannosidosis_FAQ.pdf)

Origins of the mutation

Alpha-mannosidosis appears in Angus, Galloways, and Murray Greys, it is therefore likely that the mutation originated in Scotland. The Galloway is related to the Aberdeen Angus, a breed developed in northeastern Scotland about the same time as the Galloway. A herdbook for the two black, polled beef breeds was established in 1862, with a separate Galloway herdbook opening in 1877.

(https://livestockconservancy.org/heritage-breeds/heritage-breeds-list/galloway-cattle/) Murray Greys are an Angus derivative originating in Australia. That the mutation occurs in both Angus and Galloways suggests that the mutation first occurred prior to 1877. It is logical to assume that the mutation was transported to Australia via live animals in the late 19th and early 20th centuries.

A study of the a-mannosidosis carrier Murray Grey bull. Tuerong Park Igor's pedigree reveals that all of his ancestors were in Australia's first two Murray Grey herds Thologolong and The Glen. (http://abri.une.edu.au/online/cgi-bin/i4.dll?1=223D3429&2=2434&3=56&5=2B3C2B3C3A&6=58245C592324272320&9=5B525C5F) The mutation causing alpha-mannosidosis has existed in the Murray Grey breed right from the start of the breed.

Efforts at Eradication of the Mutation in American Murray Grey Cattle

The first American awareness of the mutation came when Cranbrook Lusty tested positive. Resulting progeny can no longer be registered with the American Murray Grey Association. In 2002, the membership of the AMGA passed a bylaw requiring that all AI sires collected after January 1, 1999 must have a negative alpha-mannosidosis test result on file with the association before resulting calves could be registered. This bylaw included a "compromise" that the Board made to appease one member. Bulls collected after that date for use only in the herd of origin were exempt. There has not been a positive a-manno test result in American Murray Greys, of which the Association is aware, since testing was initiated in 2002.

Changing Conditions Require Reassessment of Rules

There was little thought given to older bulls when this bylaw was adopted. Board members at the time were not aware of how severe the alpha-mannosidosis was in Australia and they thought that Cranbrook Lusty was the only carrier bull with semen in the US. It is very likely that the AMGA management assumed that, moving forward, any Australian carrier bulls would be identified and culled before semen would be exported, and that AMGA requirements might catch any that MGBCS missed. The double check has worked well since 2002.

In the past couple of years, a Murry Grey breeder has acquired a collection of semen from some of the earlier Australian bulls imported into the US. He has provided the association with DNA markers and alpha-mannosidosis test results. Through his efforts, we learned Tuerong Park Igor and Balmoral Elation are carriers of the mutation.

The existence of the mutation in bulls drawn before Jan 1, 1999 creates a significant problem for Murray Grey breeders in the United States and for the American Murray Grey Association. As currently written, calves sired by these bulls, technically, could be registered, even with the knowledge of the carrier status of the sire. However, allowing the entry of a potential carrier could leave the breeder and the Association open to liability. It would be highly unethical to allow this to happen. That there are these 2 mutant sires from the early years of the breed raises the question of "are there more?" or perhaps better stated, "how many more are there?"

The Board of Directors of AMGA is working through the process of updating the bylaws to reflect the existence of the mutation earlier than previously thought and to do so in a way that creates the least amount of difficulty for members, while keeping the disease of alpha-mannosidosis out of the Murray Grey breed. The final proposition will likely require all AI sires to be tested and found clear of the mutation. Provisions will have to be included to try to cover as many scenarios as possible, e.g., last known straw of semen, cows bred to untested bulls at or before the time of the vote, and previously fertilized and frozen embryos, and how to deal with live progeny of older bulls that might test positive.

Any change in the bylaws of this Association will be approved by the members. All changes are dated forward, they do not take effect immediately upon ratification. And no rule or bylaw will ever penalize a member for previous actions that were accepted within the earlier bylaws but are limited, redefined, or

restricted by a new amendment. The only reason for considering a bylaw change is to forever eliminate this mutation from the Murray Grey breed.

A Greater Threat to the Industry

In 1972, when New Zealand began its a-mannosidosis eradication program, Angus genetics were represented in about a quarter of America's beef cow herd. Today, America's cow herd may be as much as 75% Angus genetics. (Personal Correspondence) The danger to the industry from an Angus genetic disease is far greater today than ever before with the extreme widespread adoption of the Angus genetics. The need to eradicate a-mannosidosis is greater now and purebred Murray Greys have a responsibility to step up and make sure that this disease can never come from our cattle. Most other Angus derived breeds are not addressing this mutation. Your breed can, and should, take the lead in eradicating alpha-mannosidosis from our gene pool.

In the past 20 years the Murray Grey breeders in the United States have moved this breed from being an "oddity" to gaining respect among the meat producing segment of the cattle business. You are poised to become a major player in America's beef production. An outbreak of a deadly disease, caused by a known, testable, and completely preventable mutation would cause horrific damage to the future of your breed. Let each of us commit to protecting this breed from a totally preventable tragedy.