Genetic Approach to Diagnosing Polysaccharide Storage Myopathy

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Genetic testing for type-1 polysaccharide storage myopathy and the modifying gene malignant hyperthermia is now commercially available. The cause of type-2 polysaccharide storage myopathy is yet unknown and requires examination of a muscle biopsy. Authors’ address: University of Minnesota, Department of Veterinary Population Medicine, St. Paul, MN 55108; e-mail: mccue0173@umn.edu. © 2008 AAEP.

1. Introduction
Polysaccharide storage myopathy (PSSM) is a debilitating muscle disease in many and diverse breeds of horses. A breeding trial of Quarter Horses with PSSM suggested that this condition was inherited as an autosomal dominant trait.

2. Materials and Methods
The diagnostic approach presented in this abstract was developed from three independent publications that were recently published or in press: (1) a whole genome association analysis of normal and PSSM Quarter Horses was used to identify the GYS1 mutation, (2) a restriction fragment length polymorphism (RFLP) assay was developed to genotype all available DNA samples from horses diagnosed with PSSM by muscle biopsy in the Neuromuscular Diagnostic Laboratory database, and (3) a genetic association study was performed on a severely affected PSSM family to identify a modifying gene.

3. Results
A dominant mutation in the GYS1 gene was identified as a cause of PSSM in these horses.1 This mutation accounts for ~80% of PSSM cases in Quarter Horses and related breeds (QHR), and has been termed type-1 PSSM.1,2 The 20% of PSSM horses from QHR that do not possess the GYS1 mutation most likely have a distinct, glycogen storage disease (type-2 PSSM).1,2 In a subset of type-1 PSSM QHR horses, the clinical severity of PSSM is modified by a second genetic mutation for malignant hyperthermia (MH);3 horses with both mutations have more severe clinical signs and poorer responses to management strategies. Although the MH mutation is present only in QHR, the type-1 PSSM mutation is found in at least 17 different horse breeds,2 and it is likely to have originated before the formation of the modern breeds known today.1 Type-2 PSSM also seems to be found in warmblood and light breeds other than QHRs.

NOTES
4. Discussion

Genetic testing for type-1 PSSM and the modifying gene MH are now commercially available at the University of Minnesota Diagnostic Laboratory. Diagnosis of type-2 PSSM will require examination of a muscle biopsy until the genetic basis for this disorder is identified. To assist practitioners in diagnosing PSSM, we have created a diagnostic decision tree based on the breed prevalences of type-1 and type-2 PSSM and MH1-3 (Fig. 1).

Disclosure of financial interest: Drs. McCue, Mickelson, and Valberg are the patent owners for the genetic testing for GYS1. A portion of the proceeds from this test will go to their continued research as well as patent royalties.

References and Footnote

3. McCue ME, Valberg SJ, Mickelson JR. Phenotype of PSSM due to GYS1 mutation is modified by the presence of an RYR1 mutation in Quarter Horses. *Neuromuscular Disorders*, accepted.