Glycogen Branching Enzyme Deficiency (GBED)

Glycogen Branching Enzyme Deficiency (GBED) in Horses

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Glycogen branching enzyme deficiency (GBED) is a disorder first recognized by clinicians at the University of Minnesota that causes muscle weakness in Quarter Horse and related breeds. The clinical presentation of this disease is variable. Late term abortion or stillbirth is described for GBED. Recent research suggests that at least 3% of abortions in Quarter horses are due to GBED. Some foals are born alive but are often weak and require warming and assistance to nurse after birth. These foals may appear healthy for a time but eventually the may develop seizures, become too weak to stand, or in some cases, they die suddenly. Owners may note that GBED foals are less active than other foals. In spite of aggressive treatment, all known cases of GBED have been euthanized or died by 18 weeks of age.

Dr. Stephanie Valberg’s laboratory recognized that foals with these symptoms have a unique muscle disease and that all these foals are related to one another. The discovery of an abnormal sugar within the skeletal muscle of these foals led the researchers to identify a genetic defect (glycogen branching enzyme gene) responsible for forming the sugar (glycogen) that provides energy for numerous tissues in the body. Now owners are able to test their horses to see if they carry this defect and this can prevent this disease from occurring. Testing can be done to determine of horses carry this genetic defect and are likely to pass it on to their offspring.

1. What is glycogen branching enzyme deficiency (GBED)?

GBED is found in Quarter Horse or related bloodlines that causes late-term abortion or death of foals by a few months of age.

2. What are the signs of GBED?

Until recently, GBED was not recognized in horses because the wide variety of clinical signs resembles many other foal diseases. The signs can be:

- Abortion or still birth of a foal.
- Weakness and low body temperature at birth. Treatment with a bottle, tubing the foal with milk, and assistance to stand and suckle regularly helps the foal become stronger.
- Sudden death on pasture of foals from the heart stopping or from seizures (due to low blood sugar).
- High respiratory rate and weakness of the muscles used to breathe in foals.
- Contracted tendons found in all four legs of a foal.
- Overall weakness and the inability of the foal to get up from lying on its side.

All foals with GBED studied to date have died or been euthanized due to weakness

3. How common is the disease?

Research done at the University of Minnesota suggests that this mutation may be present in about 10% of all Quarter Horses and related bloodlines. This means breeding carriers would result in a 25% chance of getting a foal affected with GBED. All GBED foals verified to date have been Quarter Horses and American Paint horses.
Routine postmortem examination involves having the muscle tissues examined with a stain called H&E, which does not detect GBED. Because routine postmortem exams use this stain, it is very possible that this disease has existed in Quarter Horse bloodlines for many years, but went undetected.

4. How is GBED best diagnosed?

Researchers at the University of Minnesota discovered the genetic defect and developed a test using DNA samples to determine GBED status of a horse – either affected or a carrier of the disease. At least 10 mane or tail hairs pulled out at the roots from dams or sires is preferred to test for carriers. Liver or muscle necropsy samples are preferred to determine the status of a foal.

The laboratory uses polymerase chain reaction (PCR) test on the samples. Muscle biopsies from foals affected with GBED are used for diagnosis by our laboratory. Muscle from GBED foals has a characteristic staining pattern in comparison to healthy muscle tissue.

![Biopsies from normal (left) and GBED-affected (right) horses stained with PAS. Note globules of abnormal polysaccharide with no normal background pink staining in the GBED biopsy.](image)

5. Is there a genetic test?

Yes. The University of Minnesota College of Veterinary Medicine has licensed Animal Genetics, Inc., Progressive Molecular Diagnostics, Inc., the University of California, Davis, and VetGen, Inc., to perform GBED testing.

6. Is this a genetic disease?

GBED is inherited in horses, just as in human beings. GBED is an autosomal (non-sex cell) recessive disease. This means that horses can be carriers and not show signs of the disease, but have affected offspring. Foals with disease receive an abnormal allele (copy) from both the dam and the sire.

In horses with GBED, there is a mutation in the Glycogen Branching Enzyme (GBE) gene on chromosome 26 that terminates protein synthesis.

Figure 1 illustrates the pattern of inheritance for the GBE gene:

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G= Normal allele  g= Abnormal allele

When a carrier mare (Gg) is bred to a carrier stallion (Gg), there is a 25% chance that the foal will have the disease ( gg):

When a normal mare or stallion (GG) is bred to a carrier stallion or mare Gg), there is a 50% chance that the foal will be a carrier (Gg) and a 0% chance of an affected foal (gg): Figure 2 illustrates the pattern of inheritance for normal/carrier crosses.
G= Normal allele  g= Abnormal allele

9. What abnormalities are present if my veterinarian did blood work?
Very commonly GBED foals have a low white blood cell count. They may have low blood glucose and high muscle enzymes CK and AST and the liver enzyme GGT.

8. What is glycogen branching enzyme?
The glycogen branching enzyme (GBE) is a protein that is necessary to build glycogen, the complex sugar that is a source of fuel for many tissues in the body. Normal glycogen consists of glucose (sugar) arranged to resemble a highly branched tree. GBE is the protein that arranges the branches. When a foal is missing GBE, the glycogen in its tissues lacks the normal branched structure and thus cannot effectively store sugar molecules. The tissues that rely heavily on glycogen as a fuel are skeletal muscle, heart muscle, and the brain. When foals lack GBE, these tissues become weak and unable to function properly.

9. How did you first identify GBED?
The American Quarter Horse Association funded research at the University of Minnesota to investigate the possibility that this disease existed in Quarter Horse foals. Researchers were suspicious that this disease existed after examination of muscle biopsies from affected foals. Normal muscle glycogen stains a rich pink color using a special stain called PAS. When we examined biopsies from GBED foals, we saw that there was no background pink staining. Instead, researchers saw big clumps of purple staining indicating abnormal glycogen.

The appearance of these samples was similar to the human version of GBED. Further research involved study of the glycogen structure in these samples, and found it was not properly branched.

Researchers at the University of Minnesota measured activity of the GBE enzyme and other enzymes involved in glycogen metabolism in frozen muscle, heart, and liver samples from affected foals and foals that died from other causes. There was no activity of the GBE enzyme in the foals with the abnormal appearing muscle biopsies. Our researchers also discovered that the GBE protein was absent in the tissues, confirming the suspicion the foals died because of a new disease in horses called GBED.

10. Is there a greater chance of my foal having GBED if it is a colt or if it is a filly?
No, as GBED is not sex-linked, which means that both males and females are affected equally.

11. What should I do if I think my foal has GBED?
If you want to determine if the foal has GBED, submit hair samples to the Veterinary Genetics Laboratory at the University of California Davis to test for the GBED genetic mutation. Animal Genetics, Inc., Progressive Molecular Diagnostics, Inc., the University of California Davis, and Vetgen, Inc., are now licensed to conduct this testing.

A muscle biopsy may be submitted to the University of Minnesota Neuromuscular Diagnostic Laboratory if you and your veterinarian are unsure as to whether the foal has GBED or another myopathy.

12. How do I get a test for GBED and how much does it cost?
At least 10 mane or tail hairs pulled out at the roots from dams or sires is preferred to test for carriers. Liver or muscle necropsy samples are preferred to determine the status of a foal.
13. How can I learn more about GBED?

There are several published articles and scientific papers, including the following popular press articles: