How to Use Serum Chemistries in the Evaluation of Poor Performance Thoroughbred and Standardbred Racehorses

Thomas J. Divers, DVM, DACVIM, DACVECC

Author’s address: College of Veterinary Medicine, Cornell University, Ithaca NY, 14853; e-mail: tjd8@cornell.edu © 2021 AAEP.

1. Introduction

Poor performance in racehorses is a common complaint that equine practitioners are often asked to evaluate. The poor performance might be a documented decline in performance, in which case clinical problems are plausible, or the poor performance might instead be a result of the horse never achieving owner and trainer expectations wherein searches for medical causes may be elusive. The evaluation of a poorly performing racehorse should begin with a complete history, including race records if available, and a thorough clinical examination. Endoscopic (airways and stomach) and ultrasound (thorax) examinations are often required. If the cause of the poor performance cannot be determined at this point, laboratory testing may be the next diagnostic step, and both complete blood counts (CBCs) and serum chemistry panels are recommended. The white blood cell count may provide information suggestive of an inflammatory disease, and the red blood cell evaluation provides an assessment of red cell volume and hemoglobin content, although resting equine red cell values have a wide normal range and do not reflect the values found during racing. Serum or plasma chemistry measurements should be a routine part of the poor performance evaluation in racehorses unless the history and clinical exam have already revealed an answer for the poor performance. The chemistry analytes that most often provide important diagnostic information in the evaluation of the poor performance horse are aspartate aminotransferase (AST), creatine kinase (CK), and γ-glutamyl transferase (GGT). Measurements of serum or plasma proteins, bilirubin, total carbon dioxide (CO₂), and creatinine concentrations, in addition to glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SDH) activity, may also provide important diagnostic information. The diagnostic value of each analyte is discussed below.

2. Aspartate Aminotransferase and Creatine Kinase

Abnormally high serum or plasma AST activity in racehorses is most often a result of muscle disease, although liver disease can also cause increased AST activity. If CK activity is also increased in the sample, this strongly suggests that the AST increase is a result of muscle injury. However, the absence of elevated serum CK activity in a horse with a high serum AST activity does not rule out muscle disease as a cause for the high AST because the approximate half-lives of the 2 enzymes are very different (AST half-life is approximately 7-8 days, whereas CK is approximately 2 hours). For example, if a horse worked on Monday and a transient muscle injury occurred, the initial increase in CK activity might
be in a normal reference range by Wednesday, whereas AST activity would likely remain elevated for several days. Postexercise increases in serum CK and/or AST activity are most common in horses with recurrent exertional rhabdomyolysis (RER), a disease that affects approximately 5% to 7% of Standardbred and Thoroughbred racehorses. Female horses are at a significantly greater risk for RER than males. Although RER horses can have persistently high serum AST activity, likely due to continuing subclinical episodes of rhabdomyolysis, this finding may not be predictive of performance. A combination of clinical signs (stiffness, lameness, and poor recovery following exercise) suggestive of a muscle disorder along with markedly increased serum or plasma CK activity 4 to 6 hours following a race or moderate elevations in AST actively even several days later support RER as a cause of poor performance. The timing of blood collection following exercise for the measurement of serum muscle enzyme activity is important, as serum CK activity generally peaks at 12 to 24 hours following transient muscle injury. Submaximal exercise tests that cause a 3-fold or greater increase in CK activity 4 hours after exercise can help confirm RER, but this may not be predictive of clinical expression of RER at racing speeds. Regardless, elevations in CK and AST activity following exercise warrant consideration of changes in both diet and training/racing protocols in hopes of reducing further muscle injury. Mild increases in muscle-derived enzymes in the serum may also be caused by a lack of fitness or overtraining.

3. Gamma-Glutamyl Transferase

Another common serum biochemical abnormality detected in racehorses (both Thoroughbreds and Standardbreds) is an increase in serum or plasma GGT activity above normal reference ranges, sometimes referred to by trainers and veterinarians as the “GGT syndrome”. Although the serum GGT activity in horses with this syndrome is most commonly 2 to 5 times above the normal reference range, other hepatic-specific enzymes such as SDH and GLDH and the nonspecific hepatic enzymes AST or lactate dehydrogenase (LDH) are either within the normal reference range or only mildly increased. The 2- to 5-fold increase in GGT activity often persists as long as the horse continues in full work. Studies have shown that mild-to moderate increases in GGT activity are associated with racing frequency and cumulative training load and that values return to normal when horses are removed from work. This has led to suggestions that the high GGT is caused by overtraining or maladaptation to training; the author prefers the latter term. The prevalence of the syndrome is not well documented and varies with the trainer. A recent prospective study involving three Thoroughbred stables with samples collected monthly for 5 months found the prevalence of horses that at some time point had a GGT value of >50 IU/L was nearly 15%. In that study, GGT values were as high as 127 IU/L. When high GGT activity was initially detected, the value of GGT was generally of similar or higher activity in the next monthly sample. In the author’s experience, Standardbred stables seem to have a higher prevalence of high GGTs than Thoroughbred stables. Although the increased GGT activity in affected horses is certainly abnormal, its association with poor racing performance is not well documented, and some horses with mild-to moderate-increases in GGT activity will win races. It has been suggested that GGT levels approaching 100 IU/L or greater are likely to be associated with a decline in performance. The association between high serum GGT activity and poor performance is likely increased if the horse has recently experienced any of the following: decreased weight in spite of continued normal appetite, an increase in resting heart rate, and increased time needed to cool out following training. The etiology of the GGT syndrome is unproven, but a recent case-controlled study found evidence that supported both oxidative stress and cholestasis as being involved in the syndrome. There are no controlled treatment studies to allow specific treatment recommendations, but based on a recent case-controlled study, treatments to decrease oxidative stress and improve bile flow might be reasonable. Although there is no statistical association with the equine hepatitis viruses (equine parvovirus-hepatitis [EqPV-H] and equine hepatacivirus [EqHV]) and the GGT syndrome, infection with either of these viruses should be considered as a cause for poor performance when multiple hepatic enzymes (GGT, SDH, GLDH, and AST), and especially bile acids, are increased in serum or plasma. With either virus infection, hepatitis may occur at the time of both peak viremia and increasing antibody production, suggesting that the liver disease is caused by immune attempts to clear the viruses from the liver. Chronic infection with either virus can occur, but chronic infection is unlikely to cause disease or be associated with poor performance. Paired serum qPCR viral testing 4 weeks apart will help sort out recent infection and chronic persistent infection. A decline in viremia over 4 weeks suggests that the infection is more acute and likely causative of the increased liver enzymes. Horses with hepatitis following recent infection with either virus could have a decline in performance and should not be heavily worked until the serum GLDH activity has returned to normal and the GGT is normal or approaching the normal range. If hepatic disease is being monitored by sending overnight samples to laboratories, monitoring of GLDH activity is preferred over SDH, as the latter is a less stable enzyme. When serum samples from healthy racehorses are analyzed within a few hours of racing, it is common to find mild elevations in SDH activity, and the clinical significance of this is unknown. LDH activity increases may occur with liver, skeletal muscle, or cardiac muscle...
damage. Measurement of LDH activity is included in several commercial chemistry profiles, but the low tissue specificity and its short half-life limit its diagnostic value.

4. Bilirubin
Abnormally high concentrations of serum or plasma bilirubin in horses may be caused by hemolysis, decreased appetite, or liver dysfunction. It should also be noted that a small percentage of healthy horses will have indirect and total bilirubin values well above the normal reference range without any of the above known causes. The hyperbilirubinemia in those horses may be as high as 11 mg/dl and is thought to be due to a familial deficiency of hepatic uridine diphosphate-glucuronyl transferase. A few horses with the GGT syndrome will have mildly elevated bilirubin, but this is an inconsistent finding.

5. Serum Proteins
High serum total proteins and globulins with concurrent mild decreases in albumin concentration in horses are strongly suggestive of a subacute-to-chronic inflammatory disease (e.g., lung abscess); localizing the site of inflammation can usually be accomplished by clinical exam and ancillary testing such as ultrasound exam. Decreases in albumin and total protein generally indicate an intestinal disorder. When serum protein abnormalities are found on the chemistry panel, clinical signs such as weight loss and decreased appetite are often noted along with the decline in racing performance. Although not part of a routine biochemistry panel, serum amyloid A (SAA) is a commonly used stall-side test used to detect acute-to-subacute inflammation in horses. Significant increases in SAA were not observed in healthy Thoroughbreds or Standardbreds following racing; if SAA is increased in a horse with poor performance, then an acute or subacute inflammatory disease should be suspected. SAA values might be normal if the disease process is chronic, and in one study, measurement of SAA was not helpful in the diagnosis of mild asthma in racehorses.

6. Bicarbonate, Total CO₂ and Lactate
Bicarbonate values on a chemistry panel provide an assessment of metabolic acid-base status. Some laboratories report total CO₂ (TCO₂) concentration rather than bicarbonate concentration. TCO₂ concentrations are generally 1 to 2 mEq/L higher than bicarbonate. In racehorses, pre-race TCO₂ is measured to monitor bicarbonate (“milkshakes”) administration, and pre-race values greater than 37 mEq/L (or mmol/l) suggest recent bicarbonate administration. Drug administration or medical disorders that decrease serum chloride or albumin concentrations and increase strong ion differences may also raise bicarbonate values. Furosemide administration can cause a 1- to 1.5-mEq/L increase in bicarbonate.

8. Summary
Determining the cause of poor performance in racehorses can be a diagnostic challenge. History and a complete clinical examination should always be the initial diagnostic steps. Serum chemistry analysis
should be part of the diagnostic workup when history and clinical examination do not reveal a cause. The most common abnormalities noted on chemistry analysis of poor performance horses are increased activity of muscle enzymes (CK and AST) and increased GGT activity. The time of sample collection following exercise should be considered when evaluating CK and AST values, whereas samples for GGT measurements can be taken at any time.

Acknowledgments

Funding for the investigation of the pathogenesis of high gamma-glutamyl transferase activity in the serum of Thoroughbred racehorses was kindly provided by the Grayson Jockey Club Research Foundation.

Declaration of Ethics

The Author has adhered to the principles of Veterinary Medical Ethics of the AVMA.

Conflict of Interest

Dr. Divers is Emeritus Professor at Cornell University where polymerase chain reaction (PCR) testing for EqHV-H and EqPV can be performed for a fee in the New York State Diagnostic Laboratory.

References


