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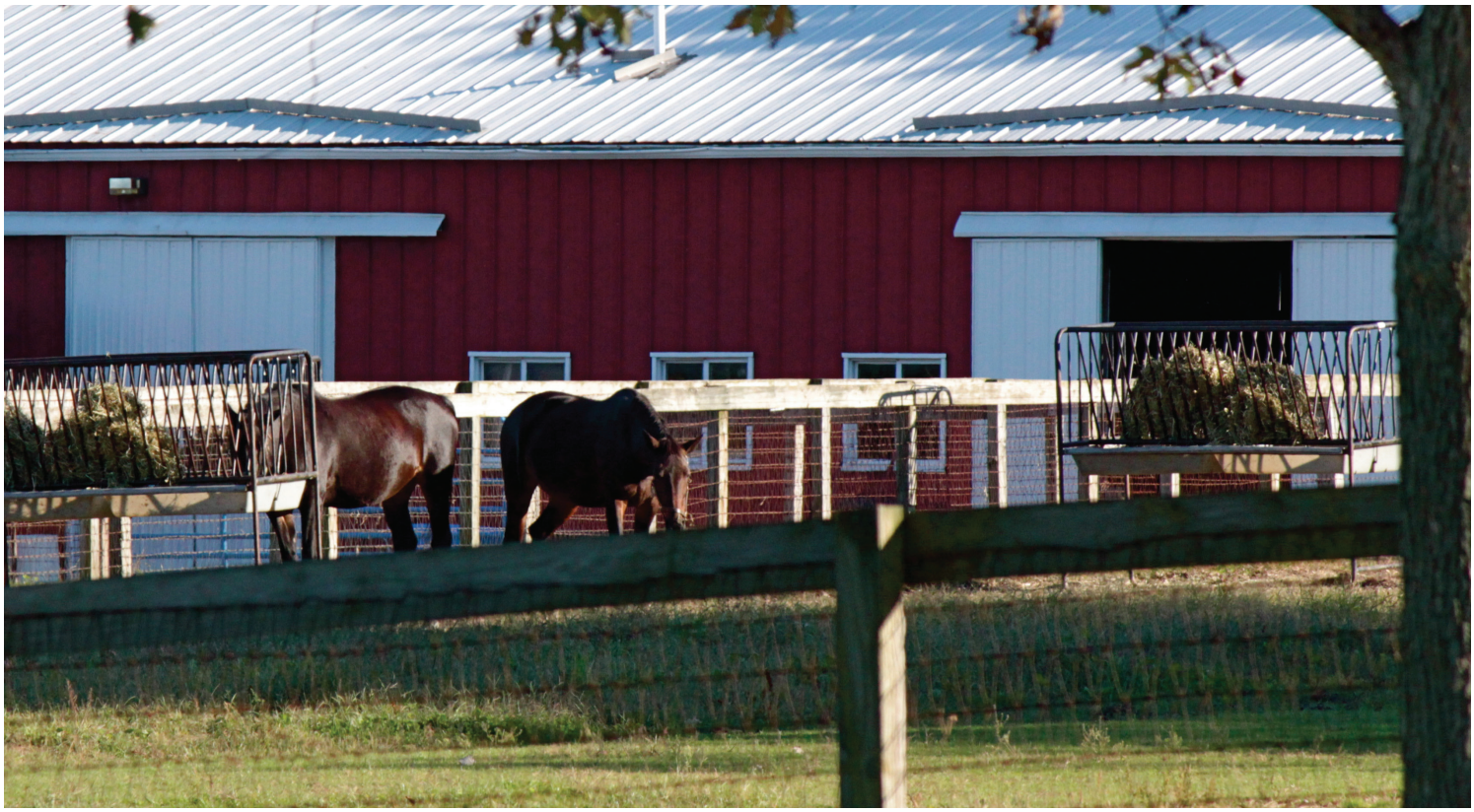
Research Updates

Evaluation of Cobalt as a Performance Enhancing Drug in Fit Standardbred Racehorses

This work was a collaborative effort between Drs. Ken McKeever and Karyn Malinowski, Professors of Animal Sciences at the Rutgers Equine Science Center and Dr. George Maylin, Director of New York State's drug-testing laboratory at SUNY, Morrisville and was funded by the United States Trotting Association.



The Research Project

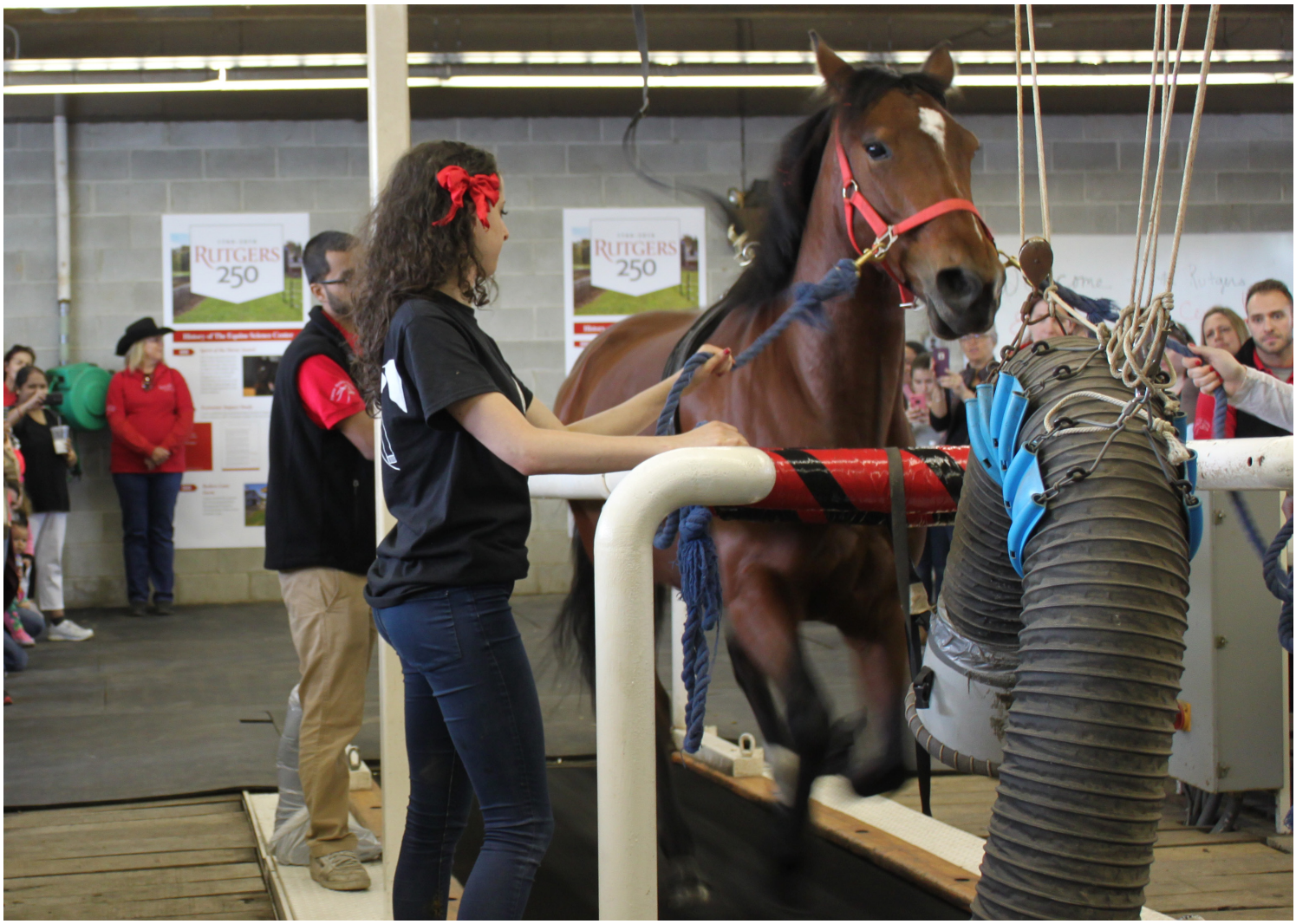
Cobalt (Co) is a trace element found in nature. It is an essential nutrient in all vertebrates.

Cobalt is required in many physiological and metabolic pathways, most noteworthy, its role as a component of vitamin B12. In addition to its role in supporting many enzymatic reactions, cobalt is involved in red blood cell production (erythropoiesis) and thyroid hormone regulation.

Generally, there is sufficient cobalt in the environment including soil, water, air and vegetation to support normal body functions in animals.

Despite the required availability of cobalt in human and animal diets, many dietary supplements and health aids contain varying amounts of the element.

Cobalt was reported to stimulate red blood cell production in the 1930s. It was used to treat



The Rutgers Exercise Physiology Lab (pictured above during Ag Field Day at Rutgers Day) was used to test the effects of cobalt administration on aerobic performance in Standardbred horses. Seven healthy, race-fit Standardbreds performed simulated race tests during the study using the equine high-speed treadmill.

pernicious anemia, aplastic anemia and sickle cell anemia in humans. Toxicity to the thyroid and heart limited the use of cobalt in the doses required to stimulate red blood cell production.

It is now known that cobalt stimulates the production of the hormone erythropoietin which activates red blood cell formation. Recombinantly engineered erythropoietin (rEPO) and similar EPO analogs, have replaced cobalt in the treatment of anemia to avoid cobalt associated toxicities.

Under normal conditions cobalt responds to a lack of oxygen in the blood (hypoxia) by causing the Hypoxia Inducible Factor 1a (HIF-1a) to increase DNA binding to the erythropoietin gene sequences and produce more EPO.

Thus, cobalt is also considered a gene doper. Large doses of cobalt administered to normal animals cause increased red blood cell production even when hypoxia does not exist. The EPO produced from cobalt is species specific.

Recently there has been renewed interest in cobalt as a performance enhancing drug (PED) in race horses and human athletes. The possible toxicity associated with its use as a PED has become a welfare concern in the horse industry.

Interestingly, a recent research study with horses demonstrated that cobalt did not affect any of the physiological parameters that were measured and it did not have any toxic effect at the dose given (Knych et al., 2014). Unfortunately, this study used a single administration rather than the multiple doses purportedly used in attempts to enhance performance.

Another unpublished report suggested that cobalt is toxic to horses when administered at 1,000 times the recommended daily allowance of approximately one milligram per horse. Racing jurisdictions have set thresholds to regulate the use of cobalt because they speculate that cobalt is toxic, and thus, constitutes a health and welfare concern.

Unfortunately, there is no unanimous agreement for a threshold at this time because dose-response studies have not been reported. Furthermore, there have been no controlled studies to document the purported performance enhancing effect of exogenous cobalt administration.

Therefore, the purpose of this study was to test the hypothesis that cobalt administration would alter biochemical parameters related to red blood cell production as well as markers of exercise performance.

Seven healthy, race-fit Standardbreds (4 geldings and 3 mares; 5±3 years of age and approximately 490 kg body weight) were used. Before receiving any drug treatment, all four completed a series of baseline testing including an incremental exercise test (GXT) to measure VO2max, biomarkers of performance, vascular volume as well as concentrations of plasma lactate, and erythropoietin. Drug administration commenced seven days after the pre-dosing GXT. Each horse was administered a sterile solution of cobalt salts (50 mg of Co HCl in 10 mL of saline, IV) at 9:00 in the morning on three consecutive days via the jugular vein. Blood samples were obtained from the contralateral jugular vein before and at 1, 2, 4 and 24 hours after administration of cobalt. Plasma and blood volume were measured one day after the last dose of cobalt; followed by a post-administration GXT performed the next day.

Horses were observed for signs of adverse effects of the cobalt administration (agitation, sweating, increased respiration, etc.). Cobalt administration increased plasma cobalt concentration from a pre-administration mean of 1.6 ± 0.6 ppb to 369 ± 28 ppb following three consecutive daily doses of the cobalt solution. There were no changes in markers of aerobic and anaerobic performance, nor any changes in plasma erythropoietin (EPO) concentration, plasma volume, resting blood volume, total blood volume, or estimated red blood cell volume.

Conclusions and Future Directions:

These results suggest that cobalt concentrations described in this research did not result in a change in biochemical parameters related to red blood cell production and did not affect exercise performance as measured by VO2max. There also were no observed adverse effects seen in the horses used in this study after the administration of 50 mg of Co HCL in 10 mL of saline, intravenously for three consecutive days.

Meet the Researchers

Dr. Ken McKeever
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Ken McKeever received his B.S. degree and M.S. degrees in Animal Science from California State Polytechnic University Pomona and Fresno State University. Following completion of his Masters he worked as the Assistant Manager of Post-Time Thoroughbred Ranch in Tulare, California. McKeever earned his Ph.D. in Animal Physiology at the University of Arizona where he also managed the University Horse Center and Quarter Horse breeding program.

Upon completing his Ph.D. McKeever served for two years as a National Academies of Sciences-National Research Council Resident Research Associate in the Cardiovascular Research Lab at the NASA Ames Research Center in California. From 1987 to 1994 Dr. McKeever developed and coordinated research at the Equine Exercise Physiology Laboratory at the Ohio State University.

In 1995 he joined the Faculty in the Department of Animal Sciences at Rutgers University as an Associate Professor and proceeded to build, develop, and coordinated one of the most active Equine Exercise Physiology laboratories in the USA. Dr. McKeever earned the rank of Full Professor in 2009 and currently serves as Associate Director of the Rutgers University Equine Science Center.

He currently serves as President of the Equine Science Society as well as the Editor-in-Chief of the journal Comparative Exercise Physiology. On a basic level his research has focused on comparative exercise and cardiovascular physiology with a particular interest in the effects of aging on the integration of the cardiovascular, renal, and endocrine systems in the control of blood pressure, blood volume and fluid and electrolyte balance.

On an applied level, his research has focused on the effects of performance enhancing practices on the physiological responses of the equine athlete. These studies are just part of the more than 200 book chapters, journal articles and proceedings papers, and more than 60 abstracts that have advanced our understanding of the athletic horse.

In his spare time, he plays water polo goalie at the local, national, and international level and is also an amateur genealogist and historian.

Further Readings:

Kinobe, R.T. 2016. Towards the elimination of excessive cobalt supplementation in racing horses: A pharmacological review. Research in Veterinary Science 104:106-112.

Knych, H.K., R.M. Arthur, M.M. Mitchell, I. Holser, R. Poppenga, L.L. Smith, M.N. Helm, R.A. Sams, C.L. Gaskill. 2015. Pharmacokinetics and selected pharmacodynamics of cobalt following a single intravenous administration to horses. Drug Testing and Analysis 7:619-625.

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