Iron: Its Functions and Metabolism in the Horse

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Iron Distribution and Storage

The distribution of iron in the horse's body is similar to that seen in humans and other mammals. The majority of biologically active iron is found complexed with hemoglobin in red blood cells (approximately 1 g iron/kg red blood cells). The iron in hemoglobin greatly enhances the oxygen-carrying capacity of blood and is a critical component of normal gaseous exchange. In fact, blood is about 60 times more effective in transporting oxygen than an equivalent volume of saline. Since transport of oxygen to the tissues is rate limiting for any athletic activity more strenuous than a 300-yard dash, the iron content of blood can be a determinant of a horse's performance.

Other than in hemoglobin, small amounts of biologically active iron are found in myoglobin (0.01 g iron/kg muscle) and in certain respiratory enzyme systems. Beyond this, iron in its storage form is complexed in ferritin in bone marrow and other sites. Iron is removed from circulation by breakdown of the red cells in the liver and spleen. Most of this iron is then released into the blood, where it combines with transferrin. Transferrin is a circulating protein that transports inorganic iron from the alimentary tract, liver, and spleen to the bone marrow, where new red cells are formed.

Iron is stored in the body as ferritin, which is a protein that can bind up 4500 iron molecules. Ferritin has a life span of only a few days and is therefore in a constant state of turnover. Ferritin is found in the cell sap, where it is called *tissue ferritin,* and also in the plasma, where it is called *serum ferritin.* Serum ferritin is produced by all the body tissues that contain ferritin, and there is a good correlation between serum ferritin and tissue ferritin levels. On this basis, serum ferritin levels are assumed to constitute a good measure of total body iron. Because ferritin is released into the plasma during inflammation, this relationship can be disturbed by disease, for example, with inflammation of a tissue such as the ferratin-rich liver.

Another storage form of iron is hemosiderin, an insoluble, iron-rich material that is believed to consist of degraded, coalesced ferritin molecules. Progressive iron loading favors the formation of hemosiderin, and hemosiderosis is a sign of long-term iron intoxication. The iron of hemosiderin is apparently readily mobilized, though, if the animal's iron intake is reduced and iron for red blood cell formation is required.

Iron Sources

Diet is the major source of iron in the horse. Iron in the diet exists in heme and nonheme forms, which tend to be poorly absorbed. Absorption of ionic iron is facilitated by low pH, which promotes the formation of stable iron complexes such as ferrous ascorbate. Ascorbic acid is therefore well known to facilitate the absorption of iron from the intestine. Nevertheless, only a small proportion of iron present in the diet is absorbed.

The iron content of the average horse is determined to be about 23 g based on estimates of the iron content of humans. Of this, about 14 g is in the form of hemoglobin, and 6 g is stored as ferritin and hemosiderin (Table I). Dietary iron intake in the horse is not reported, but based on estimates from the human literature, it is likely to be about 140 mg/day. Only about 10 mg of dietary iron is likely to be absorbed, though, with the remainder being passed in the feces. Urinary losses of iron are negligible, and it appears that a major source of iron loss is in desquamated epithelial cells or sweat. Other than these, the only other major source of iron loss in an adult horse is hemorrhage, which should be trivial in well-managed animals.

Dietary recommendations are about 40 ppm in the adult horse and 50 ppm in foals. In general, the iron needs of nonathletic horses are likely to be met by a normal balanced diet along with an iron-containing mineral lick.

Iron Loss

The major variable type of iron loss is sweat. It is difficult to be precise regarding the actual amount of iron lost in sweat because it is virtually impossible to collect a sweat sample that is not contaminated by epithelial cells. Some authors, though, have estimated that human runners can lose as much as 2 mg of iron in their sweat in the course of a marathon. From these figures, it is estimated that the daily sweat loss in humans could be as high as 6 mg, and the corresponding figure in the horse would be about 60 mg. Obvious-

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TABLE I
Estimated Iron Content of a 1000-lb Horse*

Iron Form	*Amount (g)*
Hemoglobin	14.1
Ferritin and hemosiderin	5.9
Other	2.7
Total Iron	22.7

*Figures are extrapolated from human data. The daily amount of iron required by the adult horse is set at about 40 ppm in the diet and 50 ppm for growing foals.

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ly if only 10 mg iron is absorbed each day but there is the risk of losing more than this in the sweat with hard exercise, sweating can be a significant source of iron loss in any horse that is worked hard, particularly in a warm climate.

Another source of iron loss in the exercised horse is the increased breakdown of red blood cells associated with greater metabolic and physiologic demand. This is believed to be one cause of the anemia often seen in the human endurance athlete. To compensate for this loss, human athletes in training take iron supplements. This appears to be a prudent measure in horses too, particularly if they are producing large amounts of sweat.

Hemoglobin

Iron performs the major function of transporting oxygen to the body tissues in the blood. An increase in the hemoglobin level of the blood directly increases its oxygen-carrying capacity per liter of cardiac output. The hemoglobin content of blood is thus one of the main rate-limiting factors in the efficiency of the cardiovascular system and therefore in the racing performance of a horse. Training augments both blood volume and blood hemoglobin content and thus total body hemoglobin. This occurs only if adequate iron is available and if care is taken to avoid the circumstances that can give rise to athletic anemia. This appearance of increased hemoglobin levels in the trained horse is apparently associated with the partial anoxia induced by strenuous exercise, which causes production of erythropoietin and thus increased hemoglobin production.

Theoretical considerations suggest that optimal gas transfer occurs when the mean corpuscular volume, or size, of a horse's erythrocytes is relatively small, and the hemoglobin content of the cells is high. Under these circumstances, the oxygen-carrying capacity of the red cell is high because of the high level of hemoglobin. Furthermore, smaller red cell size favors the rapid diffusion of oxygen out of the cell, leading to more efficient gas transfer. Gutschow reported that administering iron preparations to low-performance horses produced a fall in individual erythrocyte volumes, along with a simultaneous increase in the hemoglobin content of the red blood cells.[1] In Gutschow's horses, the red blood cell count and total mass increased, as well as the serum hemoglobin. Gutschow noted performance improvements after these treatments and considered high erythrocyte volumes to be indicative of a preanemic state.

Treatment with anabolic agents is another way to increase the hemoglobin content of the blood. Testosterone and the related anabolic steroids are known to increase hematocrit. Testosterone injection in a castrated male can produce up to a 20% increase in the hematocrit. This effect also occurs in females and to a lesser extent in noncastrated males, who already produce testosterone. The positive hematopoietic effect of the anabolic agents makes them the drugs of choice for most forms of anemia, and they are considered the most useful stimulants of red blood cell formation available today.[2]

Folic Acid

A second dietary factor required for red cell formation that can be deficient in racehorses is folic acid. Folic acid is required for the formation of DNA and thus for the formation of new cells. In the absence of sufficient folic acid, macrocytic anemia characterized by reduced red cell numbers and enlarged erythrocytes occurs. As discussed earlier, an enlarged erythrocyte is inefficient in the racehorse, because large red cells do not deliver oxygen to the tissues as effectively as do small red cells.

Folic acid is normally found in large amounts in fresh forage and other greens. Horses in their natural state usually have access to generous amounts of such materials, but horses at the track on the classic hay, oats, and water diet are likely to be deficient in folic acid. In a survey of Thoroughbreds in training in England, Allen found that these horses had serum folate levels significantly lower than those of mares kept on grass, and that these serum folate levels would be considered borderline for folate deficiency in humans.[3] Based on these observations, the higher folate requirements of horses in training, and their likely higher folate losses in sweat, Allen recommended that stabled horses be supplemented with about 20 mg folate/day during training and racing.

Iron Supplementation

Iron dextran injections should not be used to supplement iron. One author reported that two Thorough-

breds died within 15 hours of parenteral iron dextran injections, and in another case three horses died after the intramuscular injection of iron dextran.[4] Similarly, the administration of supplements containing iron to neonatal foals has been suggested as a cause of death. The mechanism by which iron produces tissue toxicity is unclear. It is not known whether the damage is due to ferritin; hemosiderin; or the presence of a nonferritin, nonheme compound. Earlier work suggested a classic lipid peroxidation mechanism due to an expanded intracellular iron pool with associated free-radical formation. This proposal is consistent with the known role of transferrin, which can absorb excess iron in the blood to the point of saturation. Beyond this saturation level, though, surplus iron exists in its free form in the tissues and therefore is available to damage tissue. Other workers have suggested that tissue damage is due to the excessive accumulation of iron in lysosomes, leading to rupture of these subcellular organelles, release of their lytic enzymes, and cellular death. Whatever the mechanism, iron can be toxic to tissues. Particular care should be taken in deciding the forms and amounts to be administered.

Another cause for concern with the administration of iron to animals are suggestions that iron administration can affect an animal's immune system. Many pathogens require iron for growth, and one of the possible functions of transferrin is to make circulating iron unavailable to bacteria for their growth. The clinical significance of this effect is not clear, but there have been reports of increased frequencies of infections in infants due to gram-negative organisms when the patients were given iron dextran injections. Similarly, overwhelming infections have occurred in human infants with kwashiorkor (protein deficiency) when they were given iron dextran injections. Kwashiorkor and subclinical infections are commonly found in newly weaned children in developing countries.

While these data are highly suggestive, they do not definitively implicate iron injections as a cause of increased incidence of infections. On the other hand, laboratory research has suggested that the compromising effect of iron on the immune system is due either to excess iron or to excess ferritin. Evidence has been obtained that concentrations of ferritin comparable to those observed in some disease states or after iron dextran injections can inhibit certain lymphocytic functions. Other work has suggested that reversible defects in phagocytosis can be induced. While the observations in the kwashiorkor infants are certainly suggestive, there currently is not sufficient hard scientific evidence to show a correlation between increased plasma levels of iron and an increased susceptibility to infection.

Summary

Iron metabolism is of central importance in the racehorse. Iron is directly involved in racing performance and may be in relatively short supply in a hard-working athlete due to heavy losses in sweat. Because dietary iron in a readily available form is in short supply, the amounts of iron absorbed by a horse may be only a small fraction of the actual amount needed. On the other hand, horses probably lose large quantities of iron in their sweat, and horses in training are likely to have larger turnovers of red cells than sedentary horses.

To ensure optimal iron content of the blood, it may be necessary to supplement horses with iron and folic acid. Medically, anabolic steroids are powerful and relatively specific stimulants of the hematocrit. Iron dextran injections have been reported to cause deaths in horses and should be used with care. Iron products should be avoided in the newborn foal. There may also be evidence that high concentrations of free iron in the bloodstream are associated with reduced immune function and an increased susceptibility to infection.

References

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