

Optimizing Bone Formation – Role of Nutrition, Training and Drug Interaction

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Many Variables Involved in Formation of Healthy Bone

Since the recent break down of several high profile race horses, the media and others have tried to elucidate the cause of such catastrophic injuries. Those of us directly involved in the daily management and healthcare of Thoroughbreds know that there can be many factors that cause a horse to break bones, and trying to isolate or blame just one is difficult, if not impossible. While the media has focused on such variables as the ability of some horses to pass on unsoundness to their offspring, track surfaces, running horses at two years of age and drug doping as possible causes of breakdowns, for the most part little if anything has been mentioned of the influence nutrition or training procedures have on the formation of strong, healthy bone.

There are specific nutritional and training techniques that can influence the way in which optimal bone health can be obtained and maintained. Additionally, there are several drugs commonly used in the horse industry that appear to negatively affect bone health. In lieu of the recent events, a timely discussion of bone physiology and how good quality bone is made and repaired follows. The role of nutrition and specific training techniques to enhance bone density and the effects of furosemide, phenylbutazone on calcium balance will also be discussed.

Bone is a Dynamic Tissue that Serves Structural and Other Roles

Bone is a dynamic tissue that will remodel itself in response to the forces of impact and loading. There are two types of bone tissue (fig 1). Cortical bone is dense bone that gives bones their shape and strength and comprises 80 percent of the adult skeleton. Trabecular bone is more open and porous and has a spongy appearance. Trabecular bone forms in the ends of the long bones surrounding the bone marrow and makes up the other 20 percent of bone.

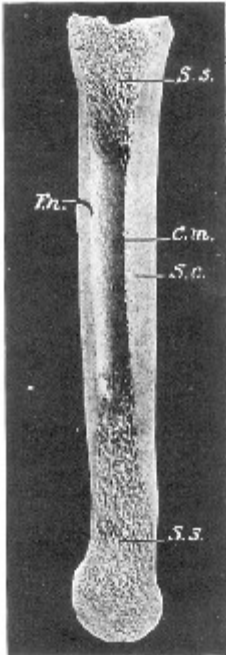


Fig 1: Cross Section of Equine Cannon Bone.

S.s. - Trabecular Bone

S.c.- Cortical Bone

C.m.- Cavity containing Bone Marrow

Taken from The Anatomy of Domestic Animals; Sisson and Grossman.

Both types of bone are made up of a matrix that has both an inorganic and organic component. Within this matrix are osteoblasts (bone producing cells) and osteoclasts (bone resorbing cells). The inorganic part of the matrix is mainly crystalline mineral salts and calcium, which is present in the form of hydroxyapatite. Mineralization of bone is achieved when osteoblasts secrete a substance containing phosphorus.

Collagen is the organic portion of the matrix . Collagen makes up 30% of mature bone and is a major component of connective tissue and cartilage and accounts for approximately one quarter of the body's protein.. Collagen gives bone a degree of elasticity and allows it to “flex” under pressure.

Osteoclasts work in unison with osteoblasts to remodel cortical bone. Both are activated when cortical bone tissue is subjected to impact and loading forces. Remodeling increases bone density by removing existing bone and adding new bone to areas where the forces are greatest. Because of this, remodeled bone is stronger than modelled bone which is bone that is laid down during normal growth periods.

The purpose of remodeling is not only to repair micro-damaged bones (from everyday stress) but also to regulate calcium homeostasis, or the level of calcium in the blood.

The process of bone resorption by the osteoclasts releases calcium stored in bone into the systemic circulation and is a critical process in regulating calcium balance. The opposite occurs as osteoblasts actively remove circulating calcium in its mineral form, taking it from the bloodstream and depositing it in bone.

Calcium Regulation is tightly controlled to maintain Blood Levels in Narrow Range

Approximately 99 percent of the calcium in the body is found in the bones and teeth and bone is comprised of about 35 percent calcium. In bone, calcium plays a structural role but serves in other functions throughout the body such as causing muscle to contract, cardiac function, blood coagulation, cell membrane function and regulation of enzymes that are needed for many biochemical reactions.

Calcium regulation in the blood is very tightly controlled because so many functions are dependent on it. A normal reference range for ionized calcium (the physiologically active form that is measure clinically) in the horse is 6.44 to 6.74 mg/dl serum. Because of this narrow range and a highly efficient process of increasing or decreasing blood calcium levels by release or uptake from bone stores, blood values do little to assess how much mineral is stored in the bone. For example, when furosemide (a loop diuretic that causes water and electrolyte loss through urine) is administered before a race, large amount of calcium as well as other electrolytes are removed from the blood. Within 15 minutes, calcium is being mobilized from the bone to replace what is lost in the blood and return the level to the acceptable range.

Simply over feeding calcium will not prevent calcium from being pulled from bone or increase the amount of calcium stored in bone. Because of tight regulation in the blood, absorption of dietary calcium will vary in order to maintain normal calcium homeostasis. Therefore, free-choice or overfeeding calcium does not “increase” stored levels of this mineral. Excess calcium will be eliminated from the body through urinary and fecal losses. However, with long-term dietary calcium deficiency, significant resorption of bone can occur, leading to decreased bone strength or abnormal bone formation, exemplifying how the body will sacrifice optimum bone strength formation to maintain the blood calcium levels, if necessary.

There are three processes that are involved in the release or uptake of calcium from bone when blood levels deviate from the normal range stated above. Vitamin D increases calcium absorption by stimulating absorption in the intestines and decreases calcium and phosphate losses by reducing urinary excretion of these minerals. It also promotes osteoclast activity, which results in demineralization or breakdown of bone.

Calcitonin (secreted by C cells in thyroid) reduces blood calcium levels by quickly (also within 15 minutes) reducing osteoclast activity by up to 70%, and increasing osteoblast number and activity. The osteoblasts begin to create new bone, incorporating calcium into their structure.

For the release of calcium into the blood, Parathyroid hormone (PTH) secreted by the parathyroid glands promotes osteoclast production and activity, while reducing osteoblast bone formation. PTH also prevents calcium loss in the urine so that blood calcium levels can quickly return to normal. The interaction of these three processes prevent hypercalcemia (high blood calcium) and hypocalcemia (low blood calcium) in a normal, healthy horse.

Other minerals are needed for bone formation

Magnesium is essential for the formation of the collagen matrix as well as bone mineralization. Around 60% of the magnesium in the body is found in bone tissue. Human studies have shown a positive correlation between bone mineral density and dietary magnesium. Low magnesium is associated with reduced activity by osteoblasts and osteoclasts.

Copper, zinc and boron are trace minerals that play an important part in bone development. Copper and Zinc are essential for bone and cartilage formation. Research in humans indicates that boron aids the uptake of calcium and magnesium into bone as well as increasing vitamin D levels.

Silicon is involved in the formation of the collagen matrix as well as bone mineralization. Silicon does not appear to become part of these tissues, but instead acts as a catalyst in the processes. The exact mechanism is not know, but it appears that silicon, when added to the diet, allows for more uptake of mineral into bone and increased production of collagen in bone and soft tissues.

Studies with horses fed silicon supplemented diets were able to train and race for longer and sustained less bone injuries than non supplemented horses. This was attributed to an overall improvement in bone density. It was noted that silicon supplementation had no effect on growth rate therefore was not connected with any risk of growth related diseases like OCD.

Silicon fed to lactating broodmares increased the levels in the milk making it available to the foal.

Mineral Availability Varies According to Source

Inorganic minerals have traditionally been used in horse feeds and are listed as oxides or sulfates on feed tags. Recently, technology that combines the inorganic mineral with an organic molecule has become an alternative to using inorganic minerals in feeds. Organic minerals are also called “chelates” or “proteinates”. Chelation involves the attachment of the mineral to an amino acid or other organic component so that the two do not disassociate in the digestive system, essentially protecting the mineral so it can be absorbed across luminal wall intact. For many minerals, a chelated compound is better than some other forms, but others absorption is not improved with complexing. For those

that are better fed as a chelate, absorption is more efficient due to a neutral electrical charge. Non-chelated inorganic minerals have either a positive or negative charge.

Because digestibility of oxides is very low, they are inexpensive to feed. Sulfates are slightly higher in digestibility but cost more to incorporate into a ration. However, organic minerals require more processing than oxides and sulfates, and are therefore the most expensive to use. There are many different forms of organic minerals and bio-availability varies depending on what type of molecule they are attached to. Most commonly, zinc, copper and selenium have higher absorption as "proteinates." Recently, studies with an organic calcium source have shown significant increases in bone density as compared to calcium carbonate, an inorganic source. Feed companies often use a combination of mineral sources, but for the most benefit organic minerals should comprise at least 25% of the total mineral supplementation.

Nutrition and training both play a role in making bone as strong as it can be.

Obviously, mineral content of the diet is important in maximizing bone density. Skeletal growth is rapid during the first 12 months of a foal's life. A thoroughbred at 6 months of age a horse can reach 84% of its mature height, whereas it may be only 46 percent of its mature weight. By 12 months it can attain 94 percent of its mature height but only 65 percent of its weight. At 22 months of age, skeletal height is 97 percent complete and 90 percent of mature weight is obtained. These numbers exemplify how much faster skeletal growth occurs than muscle accretion.

Equally as important is the level of mineralization in the bone of the growing horse. Bone mineralization begins during the last three months of gestation. At this point fetal bones are simply cartilage and contain very little mineral. The skeleton of the newborn foal contains only 17% of the adult bone mineral content. Bone mineral content (BMC) varies quite a bit while the horse is growing and is quite rapid during the first 6 months of life. At 6 months of age bone mineralization has already reached 68 percent and by 12 months it has increased to 76 percent. However, maximum BMC is not truly seen until a horse is 6 years of age.

Many factors have an effect on bone density in young horses but in addition to nutrition, exercise appears to be the most influential. Dr. Brian Nielsen, a researcher at Michigan State University has conducted numerous studies looking at the effects of nutrition and exercise on bone density and reported that exercise played a greater role in influencing markers of bone turnover than did nutrition alone. Bone formation is impacted by exercise or the lack thereof. Several studies have examined the effects of BMC in the lower legs of young horses that are stalled without access to free range exercise as compared to those that are kept on pasture. One study showed the same results even when the amount of calcium in the diet was doubled. Because the bone was in a state of demineralization from lack of exercise (and it must be sprinting, not jogging so there is enough force to make the bone remodel), it simply did not take up the extra calcium that was made available. It can be concluded from these studies that confinement to a stall causes loss of mineral from bone even when dietary supply of mineral is sufficient.

Exercise (sprinting) is the key to increasing BMC in bone. If sufficient exercise is provided, then extra dietary mineral can likely be used to improve bone strength.

Method of training and nutritional techniques can help prevent fractures

Though the training surface obviously plays a role in strengthening bone and can have a profound effect on the soundness and well being of horses exercising on it, other factors may play a larger role. A new school of thought based on the results of recent scientific studies has shown that specific training regimes, combined with precise nutritional programs can greatly enhance bone strength and density, particularly in young horses just entering training. It should be mentioned here that fear of training and racing two year olds is unjustified if the correct nutrition and training techniques are used to build optimum bone. Studies with humans have shown how influential exercise during growth can be. A 10-year study with women showed no influence of calcium intake on bone density during that period but those that exercised during adolescence had significantly increased bone mineral density and bone bending strength (determined by sports exercise questionnaire).

When a young horse comes to the track, it is generally from a training facility where it is exercised lightly with a rider in the morning, groomed and then most likely turned back out for the remainder of the day and evening. Turn out time allows the young horse to play and sprint at high speeds on its own accord, continuing to increase the strength of its growing bones. Once at the track, however, turn out time is eliminated and the horse remains in the stall except when on the track, being walked or hand grazed for a short time in the afternoon. The lack of sprinting activity, even as little as just several high speed strides once a week, begins the de-mineralization of the cannon bone. De-mineralization is a natural response to training at slow speeds, with no speed work at all.

Recent research has shown that bone becomes softest at 45-75 days (average is 60 days) after the horse has come to the track and has lived in the stall 24 hours daily. Researchers have found, however, incorporating short sprints into the training regime from near the onset of training up to day 45 helps to keep the bone from losing strength. Stopping the sprinting exercises during the critical period from 45-75 days protects the horse from potential shin bucking. After the critical period, the bone is much stronger and more equipped to handle the stress of speed work, which for most horses begins about two and half months into training (about day 75-80). See sidebar for exercise protocol to help prevent bucked shins.

Calcium absorption is decreased during critical bone remodeling period

The reason for this period of time when the bone loses mineral is directly related to calcium regulation. For currently unknown reasons, calcium absorption from dietary sources decreases at about the 64th day of training and returns to normal by 128 days of training. During the re-mineralization phase, supplementing additional calcium can help in negating the effects of decreased calcium absorption and therefore enhance the quality

of bone prior to resuming speed training. An experiment was conducted at Texas A&M to determine if additional mineral supplementation during this time would increase mineral retention and improve the strength of bone as indicated by the BMC of the third metacarpal. Twelve previously untrained Quarter Horse geldings were randomly divided into two groups. One group consisting of four horses served as controls and was fed a ration to meet National Research Council for Horses (NRC 1989, the current issue during the study) recommendations for young horses in training. Eight other horses were fed a ration that provided about 125% of NRC (1989) recommendations for calcium and phosphorus for young horses in training. Feed, feces and urine were analyzed to determine mineral absorption, utilization and retention. Radiographs were taken of the left front leg to examine bone density as indicated by radiographic bone aluminum equivalence (RBAE) Horses were broke to ride, trained to gallop on the track and maintained in training for four, 28 day periods. The high mineral treatment group had a greater increase in bone mineral content when compared to the control group. Additionally, they retained more calcium than controls at days 56 and 84, the critical time when bucked shins often occurs. An increase in calcium retention would prove beneficial in facilitating the bone remodeling process and overall skeletal growth. The authors concluded that it is beneficial to feed additional calcium to the young racehorse at the onset of training beyond NRC (1989) recommendations though the NRC (1989) recommendations for phosphorus appeared to be adequate.

Drug interaction may cause loss of calcium from bone

It was mentioned previously that furosemide results in bone calcium mobilization soon after administration in order to maintain blood calcium levels. At times, the water and electrolyte losses are so great, even homeostasis mechanisms cannot be maintained. When this happens, horses often are afflicted with what is termed "thumps" or synchronous diaphragmatic flutter. "Thumps" is seen in horses that have sweated or been depleted of water and electrolytes for prolonged time periods. Low blood calcium, potassium, and chlorine result in an increase in neuromuscular irritability and hypersensitivity of the phrenic nerve. With thumps, the beating of the heart stimulates the hypersensitive phrenic nerve to fire. This results in a contraction of the diaphragm seen at the flank each time the heart beats. Horses affected with thumps must be given intravenous calcium and electrolytes immediately to prevent sudden cardiac failure and other musculo-skeletal and neurological problems.

Whether or not the effect of furosemide has a negative effect on bone density in horses that are routinely treated with this drug is unknown. In a literature search, no studies to evaluate the effects of furosemide on BMC in horses were found (to the author's knowledge). However, several studies in humans have shown that patients treated with loop diuretics, commonly used to treat cardiovascular diseases and disorders with fluid accumulation increase show chronic bone wasting due to the excessive loss of calcium from diuresis. Though the treatment protocol is different in humans (lower daily dose) than horses, one must wonder whether horses treated with furosemide for every work and race over a racing career have lower BMC and therefore bone more prone to catastrophic failure than untreated horses.

Of equal if not more concern is the widespread use of phenylbutazone a non-steroidal anti-inflammatory drug widely used to treat pain and inflammation in horses. Several studies have shown that this drug can negatively affect bone health in horses. One study showed that oral administration of phenylbutazone for 14 days significantly decreased proteoglycan synthesis in articular culture explants (cartilage) taken from horses and should be used judiciously in athletic horses with osteoarthritis, because chronic administration may suppress proteoglycan synthesis and potentiate cartilage damage. Another study showed that yearlings treated for 30 days with phenylbutazone had decreased mineralization of the cortical bone in the tibia and a decreased rate of healing of the bone where biopsies had been obtained from compared with non treated controls. Yet another study demonstrated that phenylbutazone caused changes in biomarkers of cartilage and bone metabolism in horses. Specifically, continuous administration of phenylbutazone appeared to have an anabolic effect in healthy joints after a short period of administration. Further studies are needed to determine if the use of both furosemide and phenylbutazone negatively affect bone health in horses.

Side bar - Dietary Recommendations to Optimize Bone Density and Prevent Developmental Problems

- Fetal growth begins in utero and therefore it is important to feed broodmares adequate amounts and ratios of all required nutrients from the beginning of pregnancy. If the mare does not require a full concentrate feed (too many calories) the use of a protein vitamin mineral supplement should be used. This is a critical stage of fetal development that should not be ignored.
- Silicon should be supplemented to mares starting the last trimester of pregnancy
- Mares should be fed a concentrate ration that meets the nutrient requirements of the suckling foal since the foal will begin nibbling at the dams feed at a few days of age
- Mares fed high fat and soluble fiber rations (beet pulp, rice bran flax seed, soybean hulls, alfalfa meal) produced foals with lower incidence of Developmental Orthopedic Diseases (DOD) and also produced colostrum with higher IgG content.
- Omega 3 Fatty Acids, such as those in unrefined flax seed oil have been shown to help increase bone density by enhancing calcium absorption and reduce urinary calcium excretion.
- Some foals become insulin resistant at about three months of age until one year of age. Foals should be fed rations high in fat and soluble fiber and low in hydrolysable carbohydrate since starch and sugar have been implicated as a possible cause of DOD during this time frame.
- Weanlings and Yearlings should be kept at a moderate, steady growth rate to avoid DOD. Concentrate rations should be well fortified with good quality protein, vitamins, minerals and low in starch.
- Weanlings and yearlings should be fed separately to ensure they receive their entire ration.

- Two-year-olds in training require large amounts of digestible energy to maintain growth and provide energy for work. They may also benefit from higher amounts of calcium and phosphorus in the diet due to bone remodeling. To avoid the risk of starch overload and predisposing the horse to other metabolic disorders related to starch intake, low starch concentrates should also be fed to two-year-olds in training.
- All growing horses should have good quality forage available at all times beginning at birth. All growing horses should be provided ample turnout time to help strengthen bones and ligaments and prevent the development of some stereotypic behaviors

Side Bar - Prevention and Treatment of Shin Soreness

The schedule for adding in speed work starts with basic conditioning. Once a horse can comfortably go one mile with furlongs at 18-20 seconds each, begin introducing speed work twice a week, using a pace of one furlong (one-eighth-mile) per 15 seconds, and starting with a one-furlong distance. Every three to four weeks, increase the distance by another furlong. By the end of three months, the horse should be galloping a three-eighths-mile burst at speed, but only once every five days. On non-speed days, the horse can either be rested or jogged, or lightly galloped, allowing time for the stimulated bone to remodel. It is important to point out that the exercise program must be progressive, increasing the stress on the bone just enough to stimulate remodeling, allowing time for changes to occur, then gradually increasing the stress. The exact distances and times are least important. Training regimens that increase stress levels very quickly over a short period of time, such as when a young horse is forced to go at racing speed (or even faster than a real race) in just a few weeks such as those in preparation for a 2-year-old in-training sale, have the exact opposite effect, greatly increasing the risk of catastrophic injury.